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THE NEUROLOGICAL COMPONENTS OF METAMEMORY MONITORING: JOL ACCURACY IN YOUNGER AND OLDER ADULTS

by

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ABSTRACT

Because maximizing the learning of new material is a relevant concern for most individuals, understanding the specific processes involved could be beneficial for people of all ages. Both encoding and monitoring occur during the learning acquisition phase, yet monitoring accuracy and subsequent neural activation have been relatively ignored in the literature. The current research adapts a common metacognitive paradigm using Judgments of Learning (JOLs) to explore the neural differences in monitoring between younger (18-25) and older (65+) adults. Participants were asked to remember natural scenes and predict encoding success by providing a JOL response for each item. Participants were told to respond "will remember" if they believed they would remember that item on a later recognition memory test or "will forget" if they thought they would forget that item on a later recognition memory test. Actual memory performance was compared to predicted memory performance to provide a measure of monitoring accuracy. Individuals reported a JOL response for 150 intact (Easy) and 150 scrambled (Difficult) scenes while in a 3.0T fMRI scanner. Despite minimal differences in behavioral performance, there were several age-related neuroimaging findings of note. When compared to younger adults, older adults had decreases in medial temporal lobe (MTL) activation, as well as contralateral recruitment of the anterior cingulate. Most importantly, the present study also disambiguated structures related to encoding success (the right parahippocampus) and monitoring accuracy (the anterior cingulate). A novel account of neural structures that mediate monitoring is provided both across items

varying in difficulty (Easy and Difficult) and across different age groups (Young and Old). Encoding and monitoring are important for learning acquisition and the present research provides the first account that successfully disambiguates the two processes. Results are discussed in reference to their educational implications on resource allocation during the learning of new material.

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Be glad of life, because it gives you the chance to love and to work and to play and to look up at the stars ~ Henry Van Dyke

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Chapter 1. Introduction

Learning is a multifaceted process that can be assessed in a multitude of ways. Memory accuracy, as measured by how well individuals remember previously studied information on a later test, is one typical way to evaluate learning. While memory accuracy, or encoding success, is a vital component of learning, metamemory accuracy is also critical to learning new material. Metamemory can be defined as what an individual knows about their own memory. Metamemorial judgments involve the online monitoring of information where individuals can assess their past, present, or future performance. For example, individuals can monitor their performance to judge whether they think they have learned an item well enough to remember it on a future test. This makes monitoring an integral component of learning, specifically during the acquisition phase. Additionally, the training of resource allocation - knowing when and where to spend time in a learning situation - can be successful, and lead to higher levels of memory accuracy (Robinson, Hertzog, & Dunlosky, 2006). Interestingly, there is very little work on understanding the brain's involvement in monitoring during learning. Given that improvements in monitoring accuracy can lead to improvements in memory performance, a comprehensive look at the neural relationship between monitoring and encoding could help explain individual differences in performance and elucidate neural networks associated with learning that are distinct from structures historically linked to encoding success (e.g., hippocampus). The neural correlates associated with monitoring have been evaluated under specific conditions (e.g., judging one's confidence during retrieval attempts; e.g.,

Jing *et al*., 2004), but little is known about monitoring in relation to prospective memory judgments *during* encoding, or the learning acquisition phase.

Only one known study by Kao, Davis, and Gabrielli (2005) has attempted to identify the neurological components of monitoring during the learning acquisition phase. As will be discussed in detail, areas such as the ventromedial prefrontal cortex (VMPFC), lateral prefrontal cortex (PFC) and anterior cingulate gyrus have been associated with monitoring accuracy. The connection between the aforementioned areas and monitoring is not entirely understood and given the lack of empirical evidence, the present research aims to expand upon existing findings related to those neural correlates. In doing so, an evaluation across materials of varying difficulty and across age was completed to further substantiate the role of monitoring-related neural networks during the encoding of information.

Judgments of Learning (JOLs)

Generally speaking, the monitoring processes associated with evaluating one's own performance on a memory related task is referred to as metamemory, a subtopic of metacognition. Metamemory involves both the strategies that can facilitate successful memory formation and the processes involved in the monitoring of memory performance. Being able to accurately monitor memory performance is linked to the ability to successfully shift resources during learning where they are needed most to enhance later retention (Connor, Dunlosky, & Hertzog, 1997; Nelson & Narens, 1990). As stated by Hertzog, Kidder, Powell-Moman, and Dunlosky (2002), "monitoring provides feedback to control systems about the status of processing and processing outcome, enabling dynamic self-regulation of multiple aspects of learning" (p. 209). Metamemory research

encompasses a large domain of literature because individuals can evaluate, or assess, their memory processes during encoding phases (i.e., Judgments of Learning; JOLs), during the maintenance of information (Feelings of Knowing; FOKs), and at the time of retrieval (Confidence Judgments; CJs; see Nelson & Narens, 1990; 1994). The focus of the current research is on the memory and monitoring processes that occur during the learning acquisition, or encoding, phase.

Researchers have explored the ability of individuals to judge their own cognitive state and subsequent effects on learning and memory (Connor, Dunlosky, & Hertzog, 1997; Metcalfe & Shimamura, 1994). JOLs are a form of metamemory judgment that can be an effective way to gauge an individual's predictive accuracy for given material. These behavioral responses reflect the likelihood that the participant believes an item will be remembered on a subsequent memory test. High JOL responses would signify that the participant believes that learning has taken place and that the study materials will be remembered at a later time, while a low JOL would reflect the belief that the participant will not remember that particular item on a later memory test. Importantly, individuals are able to predict their memory performance with reasonable accuracy, meaning that JOL responses often accurately reflect the likelihood of remembering items on a subsequent memory test (e.g., Connor *et al*., 1997; Nelson & Narens, 1994).

JOL responses can be provided in a multitude of ways. A JOL response can be provided after each item is presented or after the entirety of the study list has been presented (item-by-item or global judgments, respectively). Item-by-item judgments tend to be more accurate and an effective way to look at individual differences in reference to monitoring accuracy (Connor, Dunlosky, & Hertzog, 1997). Additionally, individuals can

provide a JOL both immediately after the item is presented or after a delay. Delayed JOLs tend to be more accurate, because participants are likely to overestimate their future memory performance when responding with immediate JOLs (e.g., Connor & Dunlosky, 1991; Van Overschelde & Nelson, T. O., 2006). However, delayed JOLs have other methodological issues and do not allow for a separation of the two processes of interest to the current research (encoding and monitoring), given that monitoring takes place at a different time than the original learning. Immediate JOLs are still an effective way to gauge monitoring accuracy, as correlations are significant and participants can predict their memory above chance level. Therefore, the proposed research will incorporate immediate, item-by-item JOLs because they are compatible with fMRI scanning procedures and allow for the evaluation of both encoding success *and* monitoring accuracy while initial learning is occurring. Although there are a number of studies evaluating the neural correlates of encoding, very little information is known about the networks associated with monitoring or how monitoring and encoding are associated in the brain, if at all.

Neural Basis of Metamemory

Presently, there is little metamemory research that focuses on monitoring one's performance during the acquisition phase of learning. The JOL literature within the neuroscience domain is more sparse, but there are several papers on a type of metamemory monitoring called Feeling of Knowing (FOK) that are measured in the scanner (e.g., Jing, Niki, Xioping, & Jue-jia, 2004; Kikyo, Ohki, Miyashita, 2002; Maril, Simmons, Mitchell, Schwarts, & Schacter, 2003). Although FOKs utilize a methodology different from the JOL paradigm, and they focus on metamemory during retrieval rather

than encoding, they are still a form of metamemory monitoring that may inform the current study. FOKs refer to a judgment of "knowing" either during a retrieval attempt or after a failure to properly retrieve. For example, a participant may fail to recall specific information at a given point, but feel like that could information could be retrieved on a later test.

With so little information existing on neural correlates of metamemory, evidence from FOK studies can help identify potential regions of interest (ROIs). Neuroimaging studies of FOKs support the notion that monitoring processes can occur in areas not typically associated with encoding success. For example, FOKs typically activate areas more anterior than encoding success areas. Maril et al. (2003) compared neural activity in an event-related fMRI design in younger adults to distinguish between the neural regions associated with successful recall, unsuccessful recall, and FOKs. Scanning took place during the attempted retrieval of word pairs. Participants responded "Know" if the cued word was successfully recalled, "Feeling-of-Knowing" if the word was not recalled, but they felt like recall could be successful at a later time, and "Don't Know" if they could not recall the item and did not feel as if they would be able to do so in the future. A recognition test was administered outside of the scanner. In frontal regions, greater activation was observed for Know responses, with FOK judgments receiving less activation, and Don't Know receiving the least amount of activation. The left middle frontal cortex was activated for both Know and FOK, implying that it modulates the feeling of knowing, irrespective of successful recollection of an item. Greater activation in the left parahippocampal gyrus during encoding was associated with later successful recognition regardless of the judgment during the retrieval attempt. This suggests that

there are distinct brain areas that are related to metamemory judgments and encoding success and is an empirical step toward dissociating monitoring (i.e., FOK) from successful encoding.

In a similar vein, another imaging study was able to dissociate monitoring related areas from memory encoding related areas. Importantly, Kao et al. (2005) used a JOL paradigm and was the first to use neuroimaging to explore this type of metamemorial judgment in clinically healthy adults. Similar to the design of the present research, participants were asked to provide a JOL response while encoding natural scenes in an fMRI scanner; namely, participants made a prediction about whether they "will remember" or "will forget" for each scene. A subsequent memory test was administered outside of the scanner and these predictive judgments were compared to actual memory outcomes for each item, namely, whether the participants in fact did remember or did forget each individual item. When referencing monitoring accuracy, instances where the prediction was equivalent to the memory outcome were considered (i.e., predicting remembering when it was followed by actual remembering, and predicting forgetting when it was followed by actual forgetting). Brain regions supporting predictive JOLs were examined in relation to actual encoding success (see Appendix A for a summary of results). It was found that the lateral PFC was associated with "will remember" predictive judgments that were followed by actual remembering (called a remember-remember response; RR), separate from areas linked to encoding success. Conversely, the medial temporal lobes (MTL) supported encoding success, but not predictive judgments. Kao et al. (2005) also correlated individual JOL accuracy scores with the ventro-medial

prefrontal cortex (VMPFC) activation and found that individuals with greater activation in this region were more accurate at predicting their memory performance.

An additional study elaborated on the findings of Kao et al. (2005) using electroencephalography (ERP) because of its increases in temporal resolution, when compared to fMRI (Skavhaug, Wilding, Donaldson, 2010). Metamemory predictions in the form of JOLs were provided for word pairs while neural activation was recorded and responses were separated both by JOL predictions and memory accuracy. Between 1300 and 1900 ms, JOLs were characterized by a negative ERP effect, while memory encoding was not. According to the authors and in accordance with Kao et al. (2005), this implies that JOLs are a result of additional cognitive processing that are distinct from those that mediate successful encoding.

A very recent fMRI study has been published similarly looking at JOLs and fMRI, but using face-name pairs (Do Lam et al., 2012). Their design significantly differed from Kao et al. (2005), in that it had an encoding phase followed by a JOL phase where a retrieval attempt was possible. This was done in an attempt to disambiguate successful encoding from successful monitoring by separating the events temporally. It is important to note that this empirical design is one of merit, but evaluates a slightly different process. Providing a JOL where a retrieval attempt can be made, would be more consistent with maintenance metamemory operations (see Nelson & Narens, 1990). In agreement with Kao et al. (2005), it is the author's belief that disambiguating the two processes (encoding and monitoring) is entirely possible while both operations are simultaneously occurring. The study design in both the present research, and the Kao et al. (2005) paper allow for specific contrasts that both isolate encoding success and

monitoring accuracy. Additionally, maintenance monitoring operations are not the primary focus of the present paper, but rather acquisition related monitoring that occur in conjunction with encoding.

A limitation of Kao et al. (2005) is that they did not find a neural correlate associated with JOLs when participants predicted forgetting and subsequently forgot that item (called a forget-forget response; FF). This pattern of behavior is theoretically indicative of monitoring accuracy as much as a remember-remember response; however, no brain regions were identified as associated with forget-forget responses. This may have been a consequence of the stimuli characteristics. It is possible that the task was too easy and did not result in enough forgetting predictions to find a neural correlate associated with the aspect of JOLs related to accurately predicting forgetting. Indeed, participants in the study were both more likely to be accurate in their remember responses than forget responses (M=96, M=69, respectively) and more likely to say remember than forget (M=144, M=104, respectively). The present study intended to address this problem by introducing items that varied in difficulty, with the expectation that participants would have more judgments of forgetting for increasingly difficult items. Additionally, Kao et al. (2005) only looked at healthy younger adults. Because monitoring is an important part of learning for people of all ages, it is of interest to identify potential monitoring networks in both younger and older learners.

Thus, the goals of the current research were to explore which neural structures are associated with monitoring more generally, as well as to investigate differences in neural networks for material varying in difficulty and in the aging brain. Are there brain regions that mediate the success of monitoring despite age and despite the difficulty of material?

The present study attempted to identify a true monitoring area that mediates JOL accuracy for different materials and different age groups.

JOLs in Younger and Older Adults

What do we know already about potential age differences in monitoring during learning? From a behavioral perspective, monitoring appears to be relatively spared in both younger and older adults. For example, Robinson, Hertzog, and Dunlosky (2006) looked at the effect of generating imagery mediators for paired items and the fluency of image generation. Individuals studied paired associates and pressed a button when an image was formed. Following this, an immediate JOL was made and individuals reported the type of mediator that was generated. The ability to separate successful and unsuccessful mediator formation allowed for an evaluation of both image generation and encoding fluency. Fast imagery formation was positively correlated with JOLs, and there was no significant age difference. Importantly, both younger and older adults were able to predict their memory performance above chance levels with no significant differences between age groups, indicating age-associated spared monitoring abilities. Of interest to the present research, older and younger adults seem to be similar across more characteristics of JOLs than not (i.e., immediate JOLs, delayed JOLs, and relative accuracy of JOLs). Thus, it was expected in the current study that neural networks associated with monitoring accuracy could be identified across age groups.

Neural Basis of Memory and Aging

There are functional differences associated with age that suggest that older adults may show different patterns of brain activation when compared to younger adults, despite similarities in behavioral performance (Gutchess et al., 2005; Reuter-Lorenz & Cappell,

2008). The proposed study investigated the neural correlates of monitoring and memory encoding in younger and older adults using visual scenes. Scenes are particularly useful in discerning age-related brain differences in encoding because of their propensity to largely activate the MTL (Gutchess et al., 2005). The present study intended to disambiguate brain activation associated with encoding success and monitoring accuracy, so using stimuli that are known to activate memory areas facilitated this process.

It has been observed previously that pictures are more likely to result in increased bilateral frontal lobe activation in both younger and older adults (Golby et al., 2001; Kelley et al. 1998). However, younger adults show greater hippocampal activation than older adults while encoding scenes (Park et al., 2003). Interestingly, increases in activation have also been reported in frontal lobe regions in older adults (Gutchess et al., 2005; Logan, Sanders, Snyder, Morris, & Buckner, 2002). Because both increases and decreases in activation have been reported in older adults and can be observed in the presence or the absence of behavioral differences (Reuter-Lorenz & Cappell, 2008), the extant literature outlining the theoretical accounts of memory and the aging brain are discussed below.

How do general patterns of activation differ between younger and older adults from a strictly functional standpoint? A comprehensive meta-analysis was conducted by Rajah and D'Esposito (2005) specifically looking at age differences in PFC activation for visual and verbal episodic memory tasks. The authors wanted to be able to draw conclusions about the nature of reductions observed in the specialization of function in the frontal cortex; is it due to a systematic dedifferentiation of function, or a general deficit of function that is accompanied by some type of neural reorganization or

compensation? A dedifferentiation of function would be a result of particular areas losing specificity in regards to processing. This would explain age associated increases in activation as a spreading of function due to the lack of processing-specificity. However, in accordance with the compensation view, an absence of activation would be a result of age-related deficits in functioning (Cabeza, 2002). As Rajah and D'Esposito (2005) explain this view, "the concomitant increase in activation reflects either successful compensation for these deficits, when there are no age-differences in performance, and the 'attempted' compensation for these deficits, when there is an age-related detriment in performance" (p. 1966).

To better understand the theoretical accounts of PFC activation, Rajah and D'Esposito's (2005) meta-analysis was intended to disambiguate age-related findings observed in the prefrontal cortex. Working and episodic memory was evaluated for different brain regions by dividing the prefrontal cortex into anterior, ventral, and dorsal areas. (It should be noted that there are several ways to partition the PFC; the mentioned sections were divided because there is evidence that they are both structurally and functionally distinct from one another). When evaluating the ventral PFC, it did not appear that it was activated by older adults to the same degree as younger adults (known as "under-recruitment"; e.g., Logan et al., 2002). Although both age groups experienced a left lateralized bias, this lateralization was less apparent in older adults. Similarly, in the dorsal PFC, younger adults had greater activation overall, but in this case it seemed to be bilateral. It is suggested that older adults may under-recruit the right dorsal PFC, but over-recruit the left dorsal PFC. Older adults seem to be more bilateral in their ventral PFC activation, and less bilateral in reference to dorsal PFC activation (when compared

to younger adults). This provides evidence for a dedifferentiation of function in the ventral PFC, and a deficit in functioning in the right dorsal PFC. Consequently, there likely will not be a uniform increase or decrease in activation associated with age; that is, distinct brain areas may show different age associated changes, which is an important consideration for the present proposal.

Also, it is common to observe a dual effect of aging, whereby older adults experience both under-recruitment and nonselective recruitment of neural resources (Logan et al. 2002). Under-recruitment, where neural structures are not activated as strongly as younger adults, may occur as a byproduct of utilizing inefficient strategies. Providing older adults with an effective encoding strategy boosts both neural activation and behavioral performance, in some cases to levels similar to younger adults (Logan et al., 2002). Therefore, "unlike a decrease resulting from an irreversible absence or reduction in available recourses, under-recruitment would manifest as a context-dependent decrease that could be reversed in task conditions that encourage older adults to exploit all available resources (Logan et al., 2002, p. 828)." Conversely, nonselective recruitment occurs when neural structures not typically associated with a particular function or task are activated during experimental procedures. It may be that this occurs as a compensatory mechanism, enabling older individuals to appropriately carry out a task despite potential neural atrophy (see Cabeza, 2002; Reuter-Lorenz et al., 2001). In Logan et al. (2002), providing older adults with an effective encoding strategy reduced under-recruitment in encoding-related frontal areas, but strategy support did not affect non-selective recruitment. Even with strategy support during encoding, older adults recruited other frontal regions that are not typically activated in younger adults and are

not typically associated with encoding success. This finding is consistent with Dennis et al. (2008) and supports the notion that an anterior shift may be a result of compensatory mechanisms. However, it is not clear if nonselective recruitment of additional brain areas contributes to problems in memory for older adults or whether they are compensatory in nature.

Gutchess et al. (2005) wanted to further explore compensatory accounts of picture encoding. If neural compensation is an explanation for increases in non-selective recruitment, then the authors hypothesized greater PFC activation would be accompanied by reduced MTL activation. In other words, because the MTL is not fully active during encoding, the PFC would compensate for the decrease in activation. The neural substrates associated with incidental picture encoding were explored in younger and older adults. In reference to remembered items, both groups had bilateral inferior frontal and lateral occipital activation. Older adults simultaneously showed less activation in parahippocampal regions and more activation in the middle frontal cortex. When activation was correlated between the inferior frontal gyrus and the parahippocampus, it was found that older adults had more activation in the inferior frontal when there was less activation in the parahippocampus. Additionally, performance for older adults was similar to younger adults, with the exception that they had slightly more false alarms. This finding supports the authors' hypothesis and the notion that greater activation in the PFC could be compensatory in nature. Older adults recruited frontal regions more readily during picture encoding, leaving one to question if a similar result will be found for picture monitoring. Does what constitutes monitoring accuracy differ in younger and older adults? Although there are well-established age differences in the neural correlates

of successful memory encoding, a lack of imaging studies in aging and metacognition make an open question of whether these differences are observed during memory monitoring as well, such as when making JOLs.

To evaluate functional connectivity across age, Dennis et al. (2008) scanned both younger and older adults during the encoding of scenes, faces, and a combination of both. There were age deficits in both the prefrontal and hippocampal regions during encoding for older adults in the combination image condition. However, reduction in activation (under-recruitment) in the fusiform face area (FFA) and parahippocampal place area (PPA) were observed for all stimuli in older adults. In addition, functional connectivity between the hippocampus and posterior cortices were negatively affected by aging. However, connections with anterior regions and the prefrontal cortex were stronger in older adults. The differences in functional connectivity between younger and older adults suggest a posterior – anterior shift associated with aging that may be a result of functional compensation. This is a potentially interesting shift for the present research study, as monitoring abilities are likely to be mediated by anterior brain structures located in the PFC.

Neural Basis of Metamemory and Aging

Empirical research evaluating the neural correlates of monitoring abilities across age groups is not extensive. One type of monitoring that has been neurologically explored in younger and older adults are confidence judgments (CJs). This does not encompass a prospective evaluation of encoding success like JOLs, but rather a retrospective judgment related to retrieval confidence. The judgment is made during the test phase by asking how confident a subject is with a given answer that was provided on the test. Chua et al.

(2008) presented younger and older adults with face-name pairs. Scanning involved a mixed block event-related design that involved an encoding and recognition phase. In the encoding phase, participants were asked to learn the faces and names, and provide a non-metamemory judgment regarding the level of correspondence between the face and its paired name (i.e., "Does the name fit the face?"). During the 3 item forced choice recognition phase, participants were to indicate which name appropriately matched the face. During this block, participants also made confidence judgments by responding if they were high or low in confidence that the face on the screen matched the name they selected for that face. Both younger and older adults had greater activation for low confidence judgments in the lateral PFC, anterior cingulate cortex, and left intraparietal sulcus, when compared to high confidence judgments. Interestingly, older adults showed more high confidence errors, and did not have MTL differences in activation between high- and low- confidence responses. However, a difference in activation for high- and low- confidence responses was found for younger adults. This provides neural evidence that older adults may not be effective monitors in reference to retrieval abilities, as reflected in age-related neural differences in the MTL for high- and low- confidence stimuli and the increased number of high confidence errors.

Age Associated Methodological Considerations in Neuroimaging

Despite age-related neural differences associated with both memory and metamemory processes, certain challenges exist when comparing brain activation in younger and older adults that should be addressed in the current study. Inherent differences exist in the neural structures of older adults, compared to younger adults that could potentially make interpretations of brain findings difficult. The aging brain is

susceptible to changes that could potentially impact fMRI data. From a physiological standpoint, there may be a lag in the time it takes the Blood Oxygen Level Dependant (BOLD) signal to respond in older adults. This implies that the signal can be shifted without any experimental manipulations (Rajah & D'Esposito, 2005). Additionally, there are neurovascular changes that develop with age that can affect the amplitude of the BOLD response, as well as the signal-to-noise ratio (SNR; Rajah & D'Esposito, 2005). When the SNR ratio is smaller, as is often seen in older adults, it becomes harder to discern an actual neural response from a field of noise. White matter lesions are also more common with age and are correlated with the memory decline observed in older adults (Buckner, 2004). Estimates predict that 65% of adults 75 years of age and older suffer from white matter abnormalities (Ylikoski, 1995; cited in Buckner, 2004). Although three subjects in the present research were over the age of 75, they scored within the healthy range on the pre-screening material.

It is important to be aware of age-related differences in brain structure. Without proper measures, neural observations may simply be a consequence of cardiovascular changes associated with age and not changes in a particular process of interest. There are corrective measures that incorporate specific empirical design principles that can alleviate some of these problems. For example, rather than just looking at group differences between young and old individuals, it becomes important to introduce a within-subjects experimental variable. One can then compute statistics for interactions between age groups and the introduced experimental manipulation, rather than just looking at the overall main effects of Age that could potentially be explained by differences in neurovasculature (Buckner, 2004; Rajah & D'Esposito, 2005). In the present study, the

within subject variable of Response Type has four different conditions that allow for the evaluation of any Age x Response Type interactions. The present experimental design makes it easier to determine that observed age differences in patterns of activation are a result of experimental conditions. Using this within-subjects design, within each older adult participant, any age-related brain changes, including white matter atrophy, will be held constant because each subject serves as his or her own baseline. Consequently, observed age differences should be a result of the experimental conditions and patterns of activation can be compared between younger and older adults.

Summary of Specific Aims

The current research attempted to identify age differences associated with monitoring accuracy, both from a behavioral and neural perspective. In Kao et al. (2005), a distinct neural correlate was not found for "will forget" responses that were accompanied by actual forgetting. The introduction of an item difficulty manipulation may facilitate observations of activation in ROIs for both remember *and* forget predictions by using a procedure that will increase instances of forgetting and thereby potentially increase the power to detect neural correlates that mediate all aspects of monitoring.

There have been no previous studies on the neural components of JOLs in younger and older adults. The present experimental procedures enable the separation of two processes, encoding and monitoring, that occur simultaneously during learning. Encoding related brain activation is relatively well understood, while the neural correlates of JOLs have been less extensively researched, despite the importance of monitoring for learning. Consequently, the major goal of the present study is to contribute a more

complete picture of the neural networks that mediate monitoring accuracy in three unique ways:

1) A difficulty manipulation was introduced that was intended to identify monitoring areas that are involved in all instances of monitoring accuracy by making the task difficult. This allows for an evaluation of monitoring judgments that are related to both predicting remembering and predicting forgetting.

2) With the introduction of the difficulty manipulation, monitoring can be evaluated across both stimuli types. If regions are truly related to monitoring accuracy, then they should be active for both easy and difficult material.

3) Because older adults have relatively spared monitoring abilities, networks associated with JOL accuracy should be identified for both younger and older adults in order to create a complete picture of the monitoring networks associated with age.

Chapter 2. Methods

Participants

Both the Baylor College of Medicine and the Rice University Institutional Review Board approved the present research for human participants, who were recruited from Rice University and the surrounding community. Fourteen younger (7 males, 7 females) and 13 older adults (6 males, 7 females) were included in the analysis. Two female younger adults were excluded because there was an error in experimental procedures. Younger participants were Rice University students between the ages of 18 and 25. Older participants (65+) were contacted from a list that was obtained by posting ads in the local newspaper and community referrals. All of the younger and older adults

completed at least some college. Older and younger adults were tested at Baylor College of Medicine and were compensated 30 dollars an hour for participation. All participants were fluent in English, right handed, and had normal or corrected to normal vision. Participants did not have metal in their bodies (e.g., body piercing or metal placements resulting from surgery), were not fearful of small places (claustrophobia), and were not pregnant. The Mini-Mental State Examination (MMSE; Rovner & Folstein, 1987) was administered, with older adults averaging a healthy score of 29.55 (*SEM*=.01). Participants were given a demographic questionnaire (Appendix B), Shipley Vocabulary test (Zachary, 199; Appendix C) with words ranging in difficulty from moderately easy to moderately difficult, and a shortened version of the Memory Functioning Questionnaire (MFQ; Gilewski, Zelinski, Schaie, 1990; Appendix D). Consistent with existing literature, older adults scored better on the Shipley Vocabulary test than younger adults, although this was not quite significant (p = .12). Table 1 summarizes average ages, scores on vocabulary tests, and MMSE scores.

	Young	**Old**
Average Age	20.15	70.45
Number of Males	7	6
Number of Females	7	7
Shipley Vocabulary	32.77 (.06)	35.27 (.06)
MMSE	NA	29.55 (.01)

Table 1. Demographic information for younger and older adults. *Note:* Standard error values are in parentheses.

Materials

The study list consisted of colored scenes obtained from Oliva and Torralba (2001). One-hundred and fifty of these images were intact scenes (Easy) and 150 were

scrambled (Difficult) scenes. Another 150 items served as non-presented control items. These items were counterbalanced to create three different study lists. Within the three different counterbalances, all images were presented in the same order. Images were manipulated using Visual Basic .NET, creating nine separate segments that were randomly scrambled to create an image that would be more difficult to remember. All images had a light grey grid placed over the natural scenes; this controlled for different spatial frequencies introduced by scrambling scenes. The 450-item recognition test remained the same for all individuals. Three-hundred of those items were seen on the original study list and 150 of those items were non-presented controls. The study and test phase was programmed and executed using E-Prime® computer software.

Procedure

Outside of the fMRI scanner and prior to the collection of data, fMRI disclosures and informed consent forms were given to each participant. The experiment consisted of a study and recognition phase. The study phase took place in the fMRI scanner, while the recognition phase took place on an individual computer outside the scanner. A rapid event-related fMRI design was used to examine the relationship between predicted JOL success and actual encoding success across age (Young and Old) and item difficulty (Easy and Difficult). Individual runs were six minutes (360 seconds), and consisted of five individual runs. During each run, 60 items were presented on the screen with equal numbers of each image type being presented (30 Easy, 30 Difficult). There was a break after each run, in which subjects were told to remain as still as possible and were asked about their readiness to continue. Because neural structures associated with monitoring memory performance were of interest, only the study phase took place in the scanner.

Individual items and subsequent neural activity were then analyzed based on retrieval ability during the recognition phase. In other words, trials were sorted into four bins according to the JOL given (Remember or Forget) and the actual memory outcome (Remembered or Forgotten). This combination of responses results in four response types (FF, FR, RF, RR). The specific data analysis procedure is discussed in greater detail in the *Imaging Analysis* section.

During the study phase, participants were told to study the presented items for a later memory test. Items were presented one at a time on the screen. Additionally, during the presentation of each item, a JOL response was required. The participants gave a "will remember" or "will forget" response by pushing a button in either the left or right hand. The response associated with button pressing was counterbalanced across all participants. Participants had the full 3s to make a response, and there was a one second inter-stimulus interval (ISI) following each stimulus presentation. After 4s had elapsed, a blank screen with a fixation cross in the center was presented. Optimum random stimulus presentation (i.e., optimum timing of presentation of trials and inter-trial intervals) was determined using RSFgen (see Figure 2-3) that optimally determined the jittering schedule to minimize issues of co-linearity. Examples of the JOL procedure were shown prior to the commencement of the experimental study phase, with 10 items serving as training stimuli with extensive instructions. The training procedure occurred both outside and inside the scanner, in order to adequately prepare participants for the upcoming task. Participants were instructed to make a JOL for each individual item while the image was on the screen, and to do their best, despite task difficulty. At that time, participants were directed to ask the experimenter any questions if there are procedural ambiguities or concerns.

Outside of the scanner, participants were given a recognition memory test where they respond “Old” or “New” to images. All participants were instructed that an item was “old” if it was seen during the study phase and “new” if it was not seen on the previous study list. Participants were informed that study images would be identical to images seen at test. In other words, if a participant believed that an item was “old” it would have been presented in the same form during study (intact or scrambled). Participants were debriefed and given the contact information of the experimenter in case there were any follow up questions.

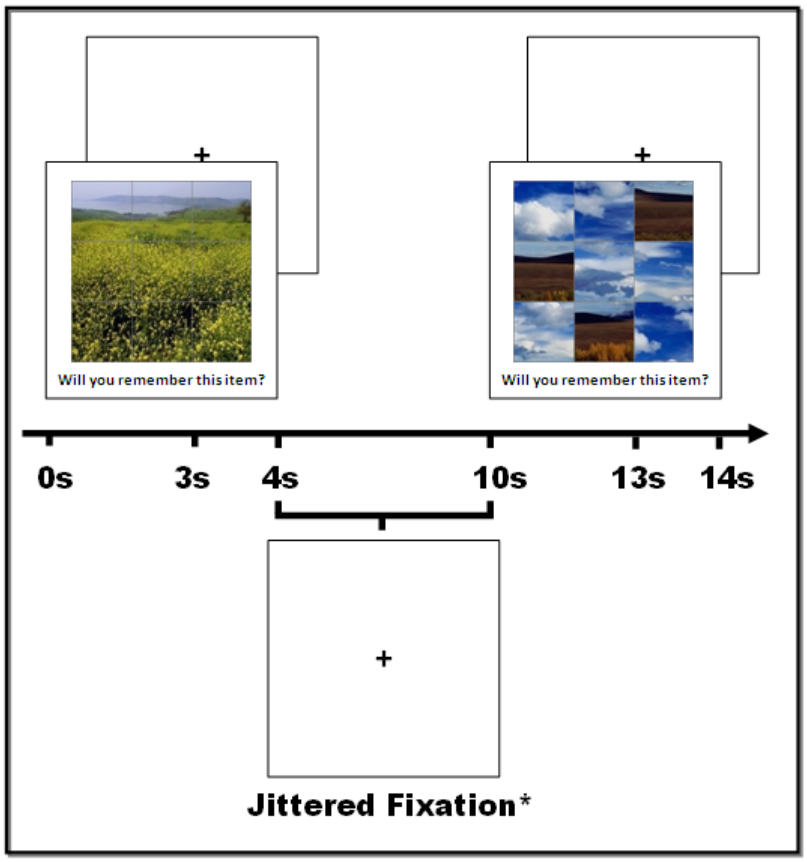

Figure 1. Schematic diagram of experimental procedures. Above is a sample of what participants may see during the study phase. It should be noted that participants will *either* see the scrambled or intact version of a natural scene, never both. *Note*: The fixation periods were randomly determined by RSFgen, and ranged between 0 and 20 seconds.

Chapter 3. Data Acquisition and Analytic Strategy

Data Acquisition

Data was collected at Baylor College of Medicine from a Philips 3T Siemans Trio scanner (software version CB15; Mark et al., 2010) with an 12-channel head coil at the Human Neuroimaging Laboratory located in Houston, TX. One hundred and ninety two, 1mm high resolution axial T1-weighted anatomical scans were obtained at the beginning of each session with a $1 \times .93 \times .93$ mm voxel dimensions (TE $= 2.66$ ms, TR $= 1200$ ms, flip angle $= 12°$, 256×224 matrix). Functional images were obtained using an echo planar imaging (EPI) pulse sequence (TE = 30 ms, TR = 2,000 ms, flip angle = 90°, 64 x 64 matrix). Twenty-nine axial slices were collected per volume, with two hundred and eight volumes collected per run. Stimuli were presented and subject responses were collected using E-prime®, and participant responses were recorded for later analysis. Stimuli were projected and viewed by the participant via a mirror mounted on the head coil.

Behavioral Analysis

The effect of age in relationship to both memory and monitoring accuracy was evaluated. This was done so by completing a signal detection theory analysis which provided a measure of accuracy (d-prime) and subject specific bias (*c*). Although there were differences in the classification of hits and false alarms for memory and monitoring, hits and false alarms were standardized and then subtracted from one another to calculate d-prime in both cases. To calculate memory accuracy, only performance on the recognition memory test was considered. Hits were classified as study items that were recognized on the memory test, and false alarms were items that were not seen during

study but falsely recognized at test (Figure 2a). For JOL accuracy, memory predictions and actual memory performance was compared. Hits were considered items that had a remember prediction and were followed by remembering on the recognition memory test and false alarms were items that had a remember prediction, but were not remembered on the subsequent recognition memory test (Figure 2b). Scores from both d-prime and criterion (*c*) were submitted to an ANOVA to evaluate the main effects of Age, Image Type, and their interaction.

A) Memory

	Responded "Old"	**Responded "New"**
Actually Old	Hit	Miss
Actually New	False Alarm	Correct Rejection

B) JOLs

	Will Remember	**Will Forget**
Remembered	Hit	Miss
Forgot	False Alarm	Correct Rejection

Figure 2. A depiction of D-Prime analysis for memory and JOLs. Each horizontal row was converted to a proportion equaling one for each subject. The values for hits and false alarms were standardized and then subtracted from one another to get a measure of accuracy (d-prime) and criterion (*c*). (A) Responding "Old" on the recognition memory test indicates that the participant believed the item was seen earlier during study. Responding "New" on the recognition memory test indicates that the participant believed the item was not seen previously. (B) Will Remember and Will Forget represent the memory prediction and Actually Remembered and Actually Forgot represents the memory outcome.

Imaging Analysis

Preprocessing

Motion correction, minimal spatial smoothing, and spatial normalization were conducted using AFNI imaging software (Cox, 1996; Medical College of Wisconsin). More specifically, afni_proc.py was used to create a processing script for each participant (see Appendix E). Outliers were identified using 3dToutcount, and censored when more than .15 of the automask voxels were outliers. 3dTshift was used to insure that the slice timing was the same for each of the 5 runs. Using align_epi_anat.py, the EPI data was then aligned to the T1-weighted anatomical scan using. Then, the anatomical scans were warped to standardized MNI space using the TT_N27 template. Individual functional runs were aligned to the initial run and then to the T1-weighted structural scan using 3dvolreg. A 4-mm full-width half-maximum (FWHM) Gaussian blur was applied using 3dmerge. A statistical model was constructed for individual participants by running 3dDeconvolve which implements general linear modeling procedures (GLM; i.e., Zarahn, Aguirre, & D'Esposito, 1997). 3dDeconvolve was used to create regressor functions and then estimate the impulse response function (IRF) separately at each voxel and across difficulty (Easy, Difficult) and for each of the four Response Types depicted in Figure 3. The deconvolution process was run twice for each subject, using the GAM and TENTzero response fitting function. The GAM option in AFNI forces the hemodynamic response to fit a curve that started at 0 and ended after 7 TRs with only one assumed peak that remains constant. A TENTzero option also confined the response function to start at 0, but with more than one assumed peak that allowed the peak response to occur at different time points. This is particularly important in aging studies, because using only a

Gamma fitting function would not allow for a proper evaluation of latency differences in the response function, as all data is fit to a curve with a single peak that occurs at the same time point. IRF output from the Gamma deconvolution process was used in the whole brain and ROI analysis to identify clusters and ROIs, respectively. However, when graphing the hemodynamic response, the output from the TENTzero option was used to provide a more accurate picture of condition differences. Instances where the participant did not respond with a JOL were included in the model as a regressor to reduce the amount of noise introduced, but excluded from any further statistical analysis because they were not a condition of interest. Omitted responses are discussed further in the *JOL Accuracy* section.

A

	Will Remember (R)	Will Forget (F)
Actually Remember (R)	Will Remember Actually Remember	Will Forget Actually Remember
Actually Forget (F)	Will Remember Actually Forget	Will Forget Actually Forget

B

	Will Remember (R)	Will Forget (F)
Actually Remember (R)	Will Remember Actually Remember	Will Forget Actually Remember
Actually Forget (F)	Will Remember Actually Forget	Will Forget Actually Forget

C

	Will Remember (R)	Will Forget (F)
Actually Remember (R)	Will Remember Actually Remember	Will Forget Actually Remember
Actually Forget (F)	Will Remember Actually Forget	Will Forget Actually Forget

D

	Will Remember (R)	Will Forget (F)
Actually Remember (R)	Will Remember Actually Remember	Will Forget Actually Remember
Actually Forget (F)	Will Remember Actually Forget	Will Forget Actually Forget

Figure 3. Response Type Combinations. Above (A) represents the combinations of Responses Types that result from the study and test phase. The column labels represent memory predictions (JOLs). The row labels represent memory outcomes. Actual encoding success, regardless of predictive judgments are represented in B. JOL accuracy can also be analyzed looking at cases where individuals said they will remember an item and actually did or when individuals responded that they would forget an item and indeed did not recognize it on the memory test (C). Finally, one can explore the relationship between remembrance responses and neurological activity, independent from prediction accuracy (D).

Whole Brain Analysis

Impulse response functions (IRFs) were generated from the 3dDeconvolve output using the GAM option and separate files were created for each condition, FF, FR, RF, RR. Individual IRF files for each condition (excluding no responses) were analyzed using GroupAna (Chen, 2010; http://afni.nimh.nih.gov/sscc/gangc/Download.html) in Matlab because of its ability to handle a four-way ANOVA (type 3): Difficulty (Easy, Difficult) x Response (FF, FR. RF, FF) x Age (Young, Old) with Subject treated as a random effects, nested variable (BxCxD[A]). Relevant first and second order contrasts were also run using GroupAna. All contrasts were corrected for multiple comparisons using a cluster size of at least 18, as needed for a voxel-wise significance of p =.01 (as determined by 3dClustSim). Further, first order contrasts were given a threshold of F = 7.78, p < .01. Using a whole brain analysis, we identified areas showing main effects between Age and Difficulty conditions. Then, functionally defined regions of interest (ROIs) were created to further explore specific condition contrasts for FF, FR, RF, and RR responses

ROI Analysis

Functionally defined ROIs were initially identified by averaging the percent signal change between 4 and 8 seconds for each participant and for each condition on the GAM deconvolution output, followed by contrasting task versus baseline at a threshold of t=5.507, p=.00001 Ignoring Age and Difficulty, theses averages were submitted to an 8 (Condition) x 27 (Subject) ANOVA using 3dANOVA2. Thirty-eight ROIs were revealed using the 3dmaxima plugin in AFNI. The x, y, z coordinates and t-statistics values are reported for the peak voxel within each ROI. The radius of each ROI was set at

5mm and a separation of 10mm from the voxel with the peak activation. Using the output from the TENTzero deconvolution process for each participant, all voxels within each ROI were averaged at each of 9 time points. Then, each ROI was subjected to a 2 (Age) x 2 (Difficulty) x 4 (Response) x 9 (Time) repeated measures ANOVA.

Given *a priori* hypotheses that the hippocampus should be sensitive to memory encoding, a bilateral hippocampus region of interest was defined by creating a hippocampus mask in AFNI. The hippocampus is an area that can be difficult to observe significant changes in signal as a result of both its anatomical location and its time course (Dennis *et al*, 2005; Rugg et al., 2002). That is, the peak activation in the hippocampus can occur several seconds after other brain regions so this anatomical ROI was identified to further evaluate brain areas associated with encoding memories. Once an anatomical mask was created, the same process that was executed on the functionally defined ROIs was repeated.

Chapter 4. Results

Behavioral Results

Because other results can be discussed in term of memory performance and JOL accuracy, this section will be broken into two sub sections. D-prime (d') was calculated for both memory and JOL accuracy, and the relevant statistics were performed on those values, unless otherwise stated. For all the behavioral results reported, the statistical significance was set at a threshold of $p \leq .05$, and is specified for each analysis. Any graphical representations of the data include +/- 1 standard error of the mean (SEM) and tables include the SEM in parentheses.

Memory Performance

Hits and false alarms were used to calculate d-prime. Hits were considered to be items that an individual saw during study and were able to remember on a later memory test and false alarms were items that the individual did not see at study but later reported seeing during the recognition test. A one way ANOVA was executed to evaluate if the between subject main effects of Age (Young and Old) was significant. Interestingly, there were no significant differences in memory performance for younger (M=.66, SEM=.16) and older (M=.78, SEM =.16) adults, $F(1, 25)= .34$, p=.57, $\eta p^2= .01$ (see Figure 4). Secondly, a repeated-measures ANOVA was executed on d-prime values, in order to test the within subject main effect of Image Type and subsequent interactions. There was an overall effect of Image Type, whereby Easy images (M=.87, SEM =.11) were more likely to be remembered than Difficult images (M=.56, SEM=.13), $F(1,25)= 9.79$, p=.005, $\eta p^2= .29$. This confirms past pilot result findings that Easy images are actually easier to remember and further validates the image manipulation as a way to create variation in memory accuracy. Figure 5 depicts this main effect. The repeated measures ANOVA rendered a insignificant Age x Image Type interaction, $F(1, 25)= 0$, p=.98, $\eta p^2= 0$ (see Figure X).

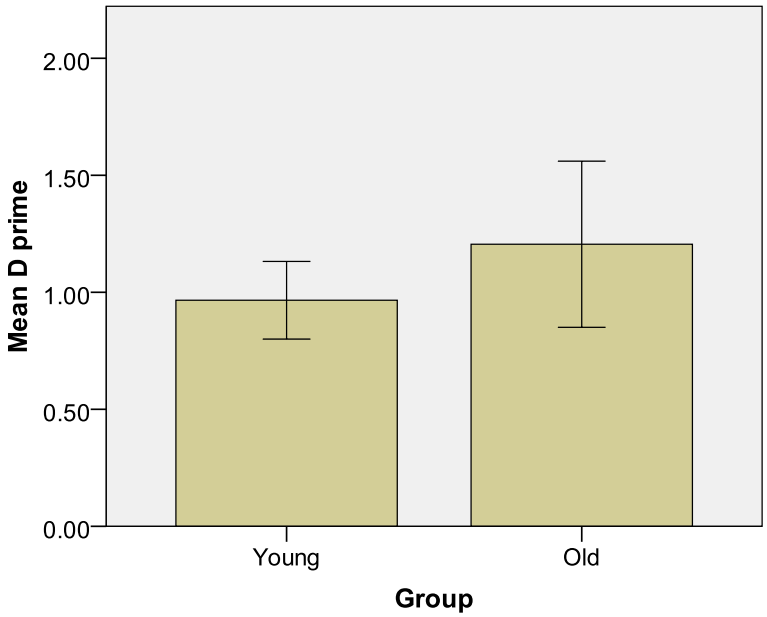

Figure 4. Memory performance for younger and older adults. When collapsing across Image Type, there are no significant differences in d-prime values for younger and older adults. *Note*: error bars represent plus +/- 1 standard error.

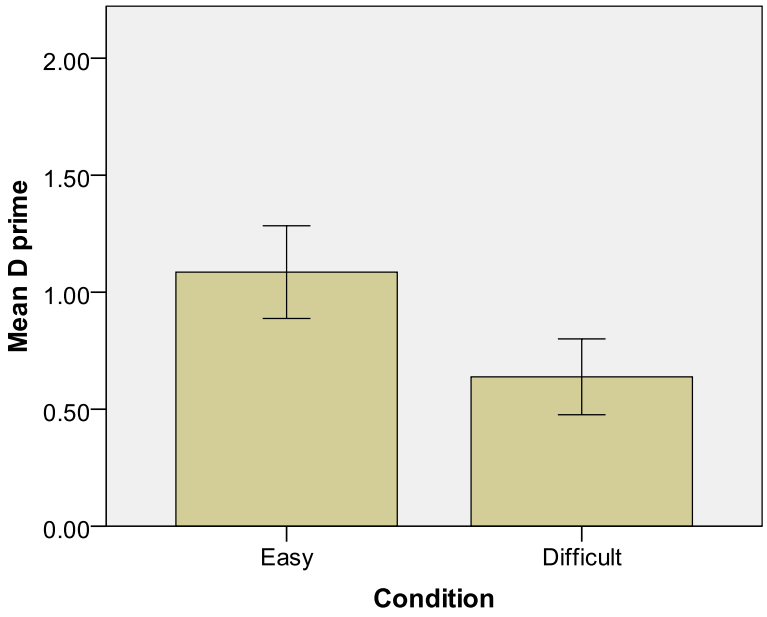

Figure 5. Memory performance for easy and difficult images. Overall, Easy images were more likely to be remembered, as determined by a comparison of means on d- prime values. *Note*: error bars represent plus +/- 1 standard error.

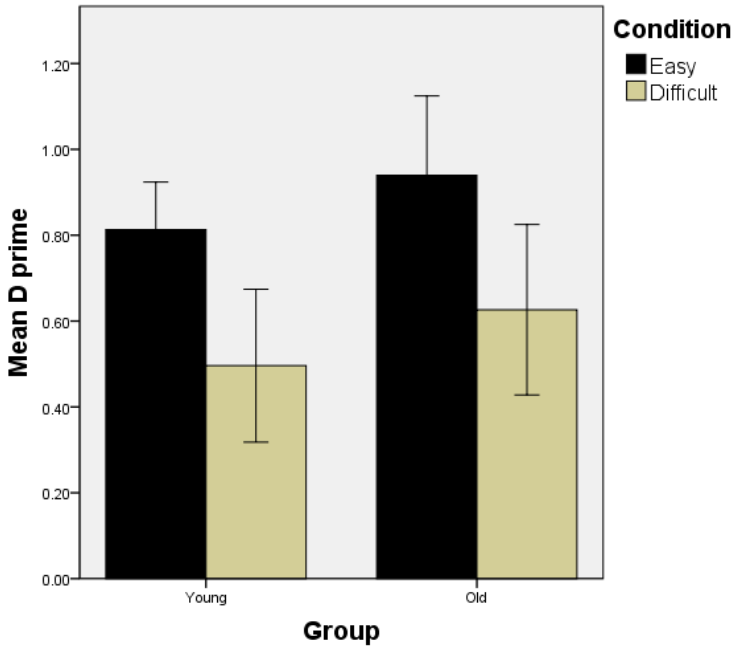

Figure 6. Memory performance across Image Type for younger and older adults. Both younger and older adults were less likely to remember scrambled items, with no significant Age x Image Type interaction. *Note*: error bars represent plus +/- 1 standard error.

For a general understanding of perceived memory functioning, the MFQ questionnaire was evaluated. Participants were asked "How often do these present a problem for you?" and an individual score was taken on 18 items, with examples such as faces and appointments (see Appendix D for the full list of questions). Participants could respond on a Likert scale with a range from 1 to 7, 1 being "always a problem" and 7 being "never a problem", so lower scores indicate greater difficulties in everyday memory functioning. Ratings from all of the questions were averaged separately for younger and older adults and subjected to a one way ANOVA. Older adults (M = 4.01, SEM = .25), when compared to younger adults (M = 4.83, SEM = .13) responded that they had more problems with memory, $F(1,26)$= 8.31, p=.008, ηp^2= .25. This is indicative of age-related perceived differences in memory functioning, despite the finding

that the behavioral results do not show differences in performance as a function of age. Consequently, older adults report more memory problems, but their performance was not a reflection of those subjective reports.

JOL Accuracy

In general, both younger and older adults were more likely to omit JOL responses for difficult images ($F(1,25)= 6.27$, $p=.01$, $\eta p^2= .23$) but older adults were more likely to omit JOL responses overall ($F(1,25)= 4.85$, $p=.03$, $\eta p^2= .17$; see Table 2). There are 4 different combinations of responses (Response Types) for younger and older adults; one can say they will remember and actually remember (RR), one can say they will remember and actually forget (RF), one can say they will forget and actually forget (FF), and one can say they will forget and actually remember (FR). RR responses are associated with both encoding success and JOL accuracy, FR responses are associated with encoding success but not JOL accuracy, FF responses are not associated with encoding success but are associated with JOL accuracy, and RF responses are associated with both unsuccessful encoding and unsuccessful monitoring. Conditions were specified after the completion of the study and determined by comparing the JOL response that was given at study to the actual memory outcome.

	Easy	Difficult
Young	0.79 (1.51)	2.24 (1.71)
Old	1.63 (2.28)	3.95 (4.20)

Table 2. Behavioral omission of responses. The above table shows the average number of omissions for younger and older adults for both the easy and difficult images. *Note*: Standard deviation is in parentheses.

Below is a table representing the proportion of responses for younger and older adults separately across Easy and Difficult conditions (see Table 3). A 2 (predicting remembering) x 2 (predicting forgetting) repeated-measures ANOVA was conducted to see if there was an interaction between the pattern of responses and Image Type (Easy, Difficult). Younger adults were both more likely to predict remembering for easy images ($F(1,26) = 13.21$, $p = .001$, $\eta p^2 = .34$) and more likely to predict forgetting for difficult images ($F(1,26) = 17.38$, $p < .0001$, $\eta p^2 = .40$). Similarly, older adults were more likely to say remember to easy images ($F(1,24) = 35.79$, $p = .0001$, $\eta p^2 = .59$) and forget to difficult images ($F(1,24) = 9.85$, $p = .004$, $\eta p^2 = .29$). This is expected, as individuals are more likely to actually remember easy images than difficult ones. Important for the present research, enough FF and RR responses are provided across item difficulty to allow for an appropriate evaluation of monitoring both during instances of predicting forgetting and predicting remembering. Without both conditions, there was not a balance of responses throughout the different cases, FF, FR, RF, RR. As expressed in Table 3, when the conditions are averaged for each age group, there are a more equal number of cases in each Response Type. Additionally, there are no longer significant differences in predictive responses (i.e., predicting remembering and predicting forgetting) for younger and older adults when JOL responses are collapsed across Image Type. This makes an evaluation of brain areas associated with encoding and monitoring more feasible, given the increase in power as a result of collapsing across Image Type.

Group	Condition	Easy	Difficult	Combined
Young	FF	.16 (.05)	.38 (.05)	.27 (.05)
	FR	.17 (.05)	.25 (.05)	.21 (.05)
	RF	.18 (.03)	.15 (.05)	.17 (.05)
	RR	.49 (.05)	.21 (.05)	.35 (.05)
Old	FF	.05 (.05)	.39 (.05)	.22 (.05)
	FR	.12 (.05)	.30 (.05)	.21 (.05)
	RF	.21 (.04)	.13 (.04)	.17 (.05)
	RR	.62 (.05)	.19 (.05)	.41 (.05)

Table 3. Average proportions of responses separated by Age and Image Type. The table shows the proportion of responses given within each response type, separated for easy and difficult images. The third column averages across image type. As can be seen, the proportions within each response type are more similar after averaging across conditions. *Note:* SEM values are in parentheses.

The accuracy of JOLs was assessed individually by comparing response predictions to actual behavioral performance and was also evaluated by using a d-prime analysis. For this analysis, hits were considered items that individuals said they would remember and were properly identified on the memory test (RR). False Alarms were items that individuals said they would remember, but actually forgot during the memory test (RF). This provides an objective measure of JOL resolution; that is, how well individual participants can predict memory performance for individual stimuli. There was not a main effect of Age, (Figure 7), as both young (*M*=.97; *SEM*=.15) and old (*M*=.84; *SEM*=.13) were similarly able to monitor their memory performance. Additionally, when completing a repeated-measures ANOVA on easy and difficult d-prime scores, a significant effect of Item Difficulty was not observed (see Figure 8), as participants could predict their memory performance similarly for easy (*M*=1.07; *SEM*=.11) and difficult (*M*=.82; *SEM*=.13) images. It should be noted that, although there is no significant difference in JOL accuracy for Easy and Difficult images, with additional subjects

significant difference between Image Types might be observed. In past pilot testing, the main effect of Image Type is significant, but this is likely not observed because of a lack of power due to the number of subjects. There was a significant Group x Difficulty interaction, $F(1,25)= 4.07$, $p=.05$, $\eta p^2= .14$. As can be seen in Figure 9, older adults had a more difficult time monitoring their memory performance for difficult images. This may be explained by the observation that older adults were more likely to underestimate performance (say forget and actually remember) for the difficult stimuli and could be reflective of a difference in strategy and/or feelings of competency (self-efficacy) that shift their response bias (Bandura, 1982; 1989). This can be better understood when evaluating measures of criterion shifts associated with signal detection theory.

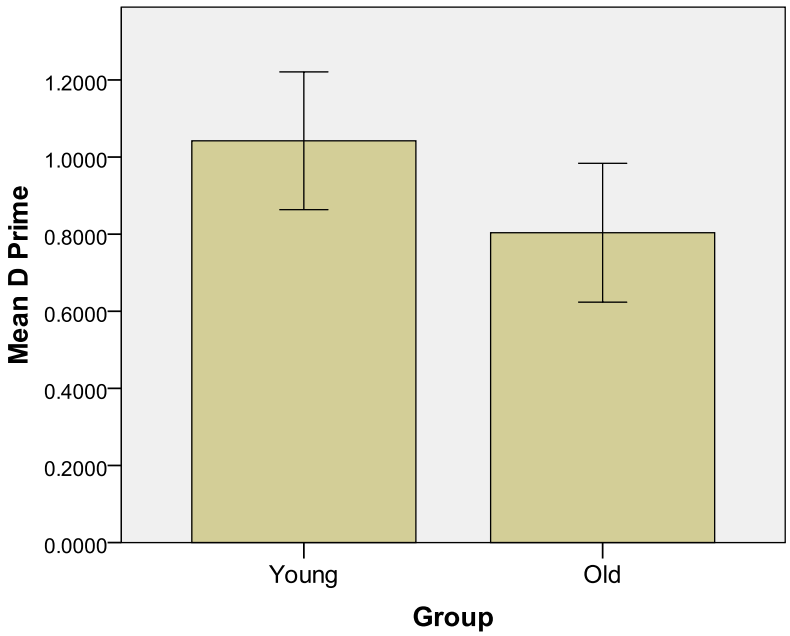

Figure 7. JOL accuracy for younger and older adults. There were no significant differences between younger and older adults ability to predict memory performance, when collapsing across image type. *Note*: error bars represent plus +/- 1 standard error.

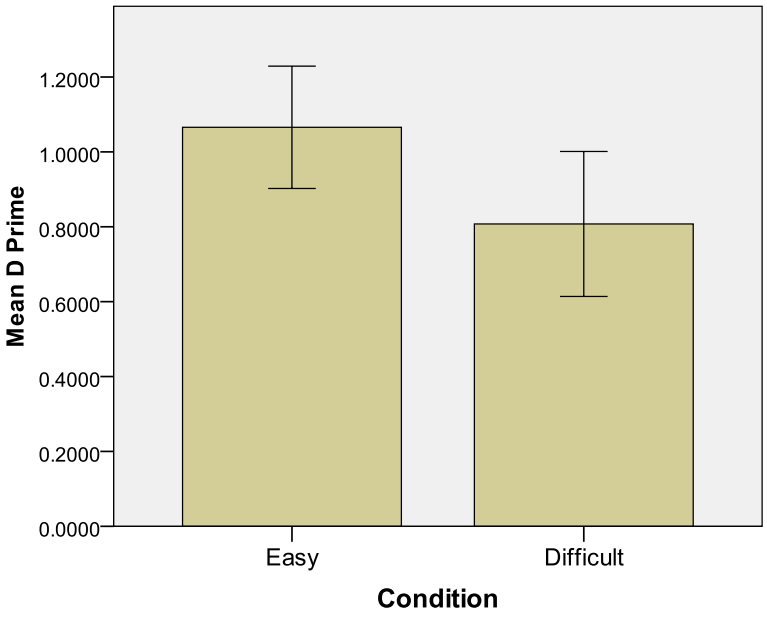

Figure 8. JOL accuracy for easy and difficult images. There were no significant differences between easy and difficult images, when collapsing across age. *Note*: error bars represent plus +/- 1 standard error.

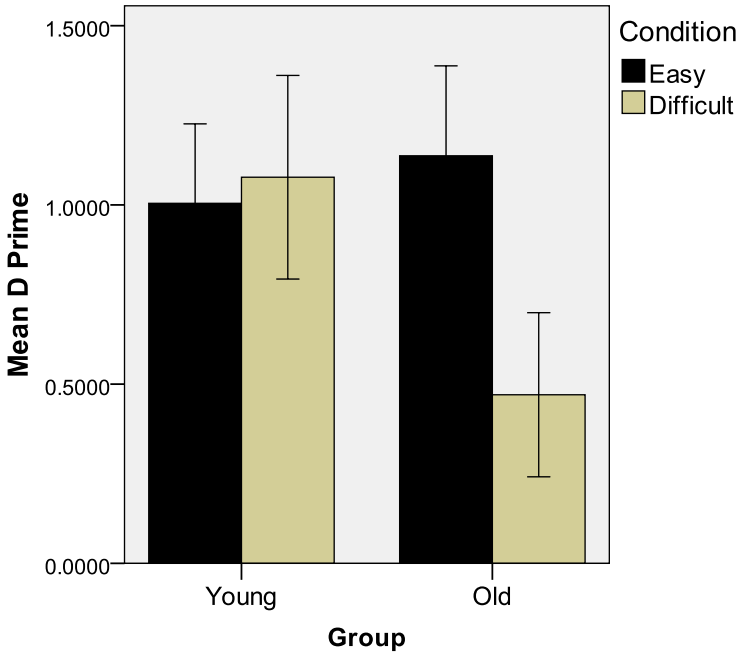

Figure 9. JOL accuracy across Image Type for younger and older adults. There was a significant interaction, in which older adults had a more difficult time predicting memory performance for difficult images. *Note*: error bars represent plus +/- 1 standard error.

In addition to d-prime, estimates of criterion (*c*) were evaluated. Criterion is a secondary measure associated with signal detection theory that is reflective of internal biases or a propensity towards a specific type of responding. When *c* is in the positive direction, it indicates a more conservative pattern of responding. In the case of the present experiment, a positive *c* would be characteristic of a participant who did not say "will remember" as often. The converse is true; if a participant has a negative *c* value, it is indicative of liberally responding "will remember". Individuals were more likely to be liberal on easy images (*M*=-1.17) and conservative on difficult images (*M*=.53). When conducting a repeated measures ANOVA, this effect of Image Type is highly significant, $F(1,26)= 19.162$, $p<.0001$, $\eta p^2= .45$. Further, when compared to younger adults, older adult responding is more conservative for difficult images and more liberal for easy images, rendering a significant Gender x Difficulty interaction, $F(1,26)= 5.85$, $p<.02$, $\eta p^2= .20$ (see Figure 10).

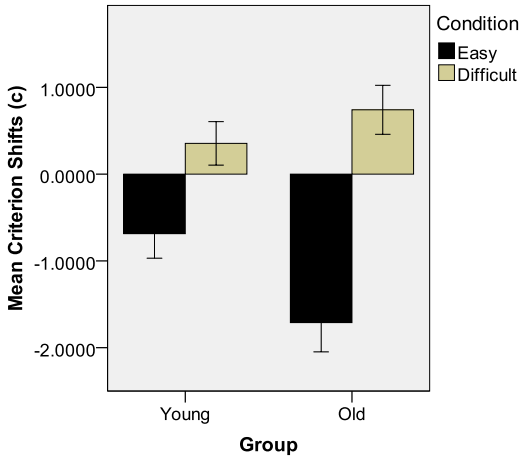

Figure 10. Criterion shifts across Image Type for younger and older adults. Participants are more likely to be liberal in responding for easy images and conservative in responding for difficult images. This interaction was significant across age groups. *Note*: error bars represent plus +/- 1 standard error.

Whole Brain Analysis

A whole brain approach was used to evaluate the main effects of age and image type. A 4-way ANOVA was conducted in conjunction with a series of subsequent *t*-tests. It should be noted that the design was unbalanced because of a different number of subjects in each age group. GroupAna has the capability of handling unbalanced ANOVAs, and the current design did not violate any known assumptions. Numerous statistical analyses can be discussed; however, only interactions and contrasts that test *a priori* hypotheses are reported to reduce the likelihood of committing Type 1 errors. Consequently, results from the 4-way ANOVA that address effects of Age and Image Type are discussed separately. All coordinates are reported in the Montreal Neurological Institute (MNI) standardized space.

Effects Associated with Age

As evident from the existing functional neuroimaging literature, younger and older adults are expected to differ in overall brain activation. For example, increases in brain activation have been found across numerous brain regions (specifically frontal), both with and without age differences in performance (Reuter-Lorenz & Cappell, 2008). Consequently, an analysis of general age-related differences was conducted. See Figure 11 for a pictorial representation of the Young versus Old contrast. When completing the first order contrast of Young versus Old, only one area revealed significantly greater percent signal change for younger adults with a threshold of $F = 7.78$, $p < .01$ (corrected) located in the lingual gyrus, a posterior region associated with processing visual stimuli (x = 14, y = -81, z = -13). Upon further inspection, one can see that this area differed

significantly across age because younger adults had a negative percent signal change (or deactivation; see Appendix F for the hemodynamic response function).

Interestingly, 14 regions were associated with greater percent signal change in older adults. Table 4 has the full list, including x, y, z coordinates, *t*-values, anatomical regions and their corresponding BAs. Of those regions four were located in the parietal lobes, one in the occipital lobe, one in the temporal lobe, and eight in the frontal lobes. Eight frontal regions were characterized by a greater change in activation in older adults when compared to younger adults that included the right inferior frontal gyrus (BA 9), left middle frontal gyrus (BA 8/9), and the bilateral medial frontal gyrus (BA 6). Upon further examination of the frontal regions, the percent signal change was significantly greater in older adults when compared to younger adults (See Appendix G). This is consistent with both previous reports of greater activation levels in older adults (Reuter-Lorenz & Cappell, 2008) and the observation of a posterior to anterior shift of activation associated with age (Davis et al, 2008; Gutchess et al., 2005).

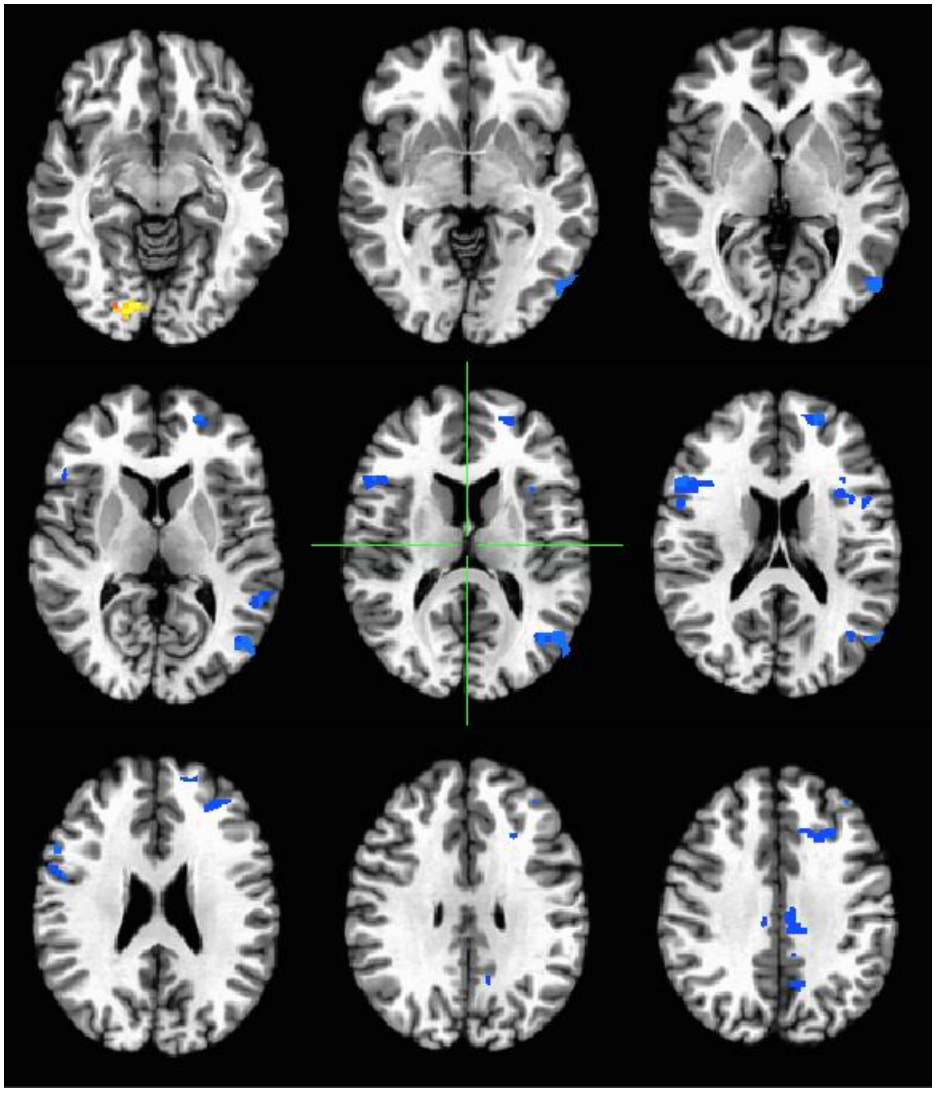

Figure 11. Whole brain results from the Young versus Old contrast. Red/yellow signifies areas where younger adults had a greater change in signal, while the blue signifies areas where older adults saw a greater change in signal. This was a first order contrast, set at a threshold of t=2.786, p = .01. The cluster size was set at 18, correcting for multiple comparisons at p=.01 Mean gamma IRFs were used for this analysis.

Effect	MNI Coordinates x	y	z	*t*-value	Cluster	Hemi	Region	BA
Young > Old	14	-81	-13	3.99	36	R	Lingual Gyrus	18
Old >Young	19	54	21	4.30	36	R	Middle Frontal Gyrus	10
	-28	25	39	4.01	37	L	Middle Frontal Gyrus	8
	41	-44	59	3.81	267	R	Post Central Gyrus	5
	-4	-40	42	3.71	90	L	Cingulate Gyrus	31
	-1	-16	57	3.67	20	L	Medial Frontal Gyrus	6
	-49	-72	-5	3.55	86	L	Middle Occipital Gyrus	19
	-34	41	37	3.48	18	L	Middle Frontal Gyrus	9
	-34	-56	58	3.24	240	L	Superior Parietal Lobe	7
	-53	-48	6	3.22	19	L	Middle Temporal Gyrus	21
	51	1	25	3.13	18	R	Inferior Frontal Gyrus	44
	54	20	23	3.10	60	R	Inferior Frontal Gyrus	44
	-31	14	16	3.10	22	L	Inferior Frontal Gyrus	44
	8	-13	50	2.90	52	R	Medial Frontal Gyrus	6
	-7	-68	35	2.85	21	L	Precuneus	7

Table 4. Significant clusters associated with the Young versus Old contrast. Clusters were set at a threshold t=2.786, p = .01. The cluster size was set at 18, correcting for multiple comparisons at p=.01 *Note*: Clusters appear in order of magnitude of the *t*- values extracted from the peak voxel in each cluster. L = left, R = right.

Age Effects Associated with Image Difficulty

The initial ANOVA revealed five significant clusters (see Table 5) that were associated with an Age x Difficulty interaction and were located in frontal regions. Given this interaction, IRFs were extrapolated from the significant clusters by averaging the percent signal change at each time point and from each subject for all the voxels contained within that cluster. Of interest, the right cingulate gyrus was associated with a greater activation in older adults when compared to younger adults for easy images, while younger adults had greater activation in this region when compared to older adults in the

difficult condition (see Figure 13). Second order contrasts between young and old were completed at each level of the difficulty manipulation to further explore age and image type effects (Easy and Difficult) and can be viewed in Appendix H. For easy images, five areas resulted in a greater percent signal change for younger adults: one was located in the parietal lobe, three in the occipital lobe, and one in the cerebellum. Thirteen areas resulted in a greater percent signal change for older adults for easy images with four located in the parietal lobes, two in the occipital lobes, one in the temporal lobe, and six in the frontal lobes. When looking at difficult images, more areas were located in posterior regions of the brain. Younger adults had a greater percent signal change than older adults for four occipital regions and one temporal region. Older adults had greater activation in three parietal regions and three occipital regions. There were three observations to note from the second order contrasts. First, younger adults recruited more posterior regions, compared to older adults. Second, older adults recruited numerous frontal regions, while there were no frontal regions in which younger adults had greater activation. Third, for both age groups, there were more significant clusters located in posterior regions for difficult images than for easy images.

	MNI Coordinates							
	x	y	z	*F*-value	Cluster	Hemi	Region	BA
Age x Difficulty	44	-13	1	15.82	54	R	Insula	13
	23	15	52	13.69	18	R	Middle Frontal Gyrus	6
	4	23	27	10.47	68	R	Anterior Cingulate	32
	-43	-14	11	10.33	49	L	Insula	13
	-19	9	52	8.28	19	L	Medial Frontal Gyrus	6

Table 5. Significant clusters associated with an Age x Difficulty interaction. The Threshold was set at t=2.786, p = .01, rendering five regions that had a differential pattern of activation associated for difficulty (Easy, Difficult) across age. *Note*: Clusters appear in order of magnitude of the *F*- values extracted from the peak voxel in each cluster. L = left, R = right.

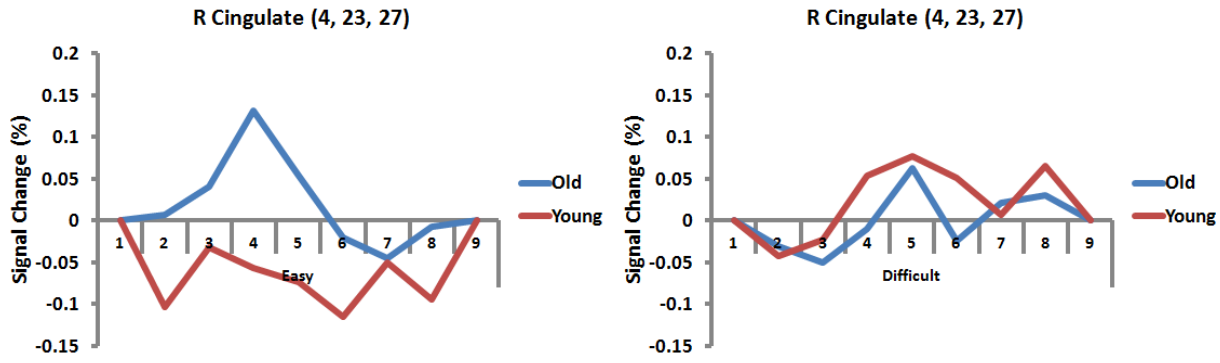

Figure 12. The hemodynamic response in the right cingulate. Older adults recruit the right cingulate more than younger adults when presented with easy images. X, Y, Z coordinates are in parenthesis.

ROI Analysis

An ROI analysis was conducted in order to identify regions associated with monitoring accuracy, encoding success, and confidence. Using the procedure described in the Method under *ROI analysis*, 38 ROIs were identified in the task versus baseline contrast with a threshold $t = 5.507$, $p = .00001$. Of those regions, 6 were located in the parietal lobes, 5 in the occipital lobe, 8 in the temporal lobe, and 14 in the frontal lobes. The remaining 5 regions were located outside of the cortex, in more medial structures. Following this, a 2 (Age) x 2 (Difficulty) x 4 (Response) x 9 (Time) repeated measures ANOVA was conducted on all ROIs. A report of the coordinates, anatomical area, z-scores, and the significant main effects and interactions for all ROIs can be seen in Appendix I. Given that general effects of Age and Image Type were discussed in conjunction with the whole brain analysis, only ROIs involving an effect or interaction of Response will be discussed. Specifically, because monitoring accuracy (RR, FF), encoding accuracy (RR, FR), and predicting remembering (RF, RR) are of primary interest, three contrasts were performed on all ROIs that had at least one of the following significant effects: Response, Response x Age, Response x Time, Response x Age x Time. Percent signal change was averaged between TR 3 and 5 for each response type (FF, FR, RF, RR) and the relevant t-tests were performed on the contrasts of interest. The easy and difficult images were averaged together for each response type, as the primary purpose of the difficulty manipulation was to create enough cases in each response cell, not to evaluate effects of difficulty level. Highlighting these interactions focuses the attention of the ROI analysis on its intended purpose, which was to identify regions unique to monitoring, encoding, and predicting remembering. The initial contrasts for

each ROI were completed by collapsing across age, and then subsequent contrasts were conducted separately for younger and older adults to see if the same pattern was observed individually for both age groups.

Brain Regions that Mediate Remember Judgments

Responses of "will remember" are not contingent upon actually remembering an item and therefore encompass instances where one predicts remembering and subsequent remembering occurs for that item (RR), or where one predicts remembering and subsequent remembering does not occur for that item (RF). Initial analyses of pertinent brain areas were executed collapsing across age. Initially, the left precuneus (x = -28, y = -55, z = 41) rendered a significant Response x Time interaction ($F(21,5)= 15.99$, $p=.005$, $\eta p^2= .65$). Because of this interaction, the RR and RF versus FR and FF contrast was executed and found to be significant ($F(1, 26)=7.72$, $p = .01$). There was not a significant Age x Response interaction ($F(3, 23)=.19$, $p = .67$) implying that this is an area that mediates confidence in remembering regardless of one's age. Additionally, the right precuneus (x = 26, y = 67, z = 32) rendered a significant result for the aforementioned contrast ($F(1, 26)=6.86$, $p = .01$). Similar to the left precuneus, there was not a significant Age x Response interaction ($F(3, 22)=.1.64$, $p = .21$. See Figure 13 for a summary of these results. In sum, the bilateral precuneus appears to mediate predictions of remembering for both younger and older adults.

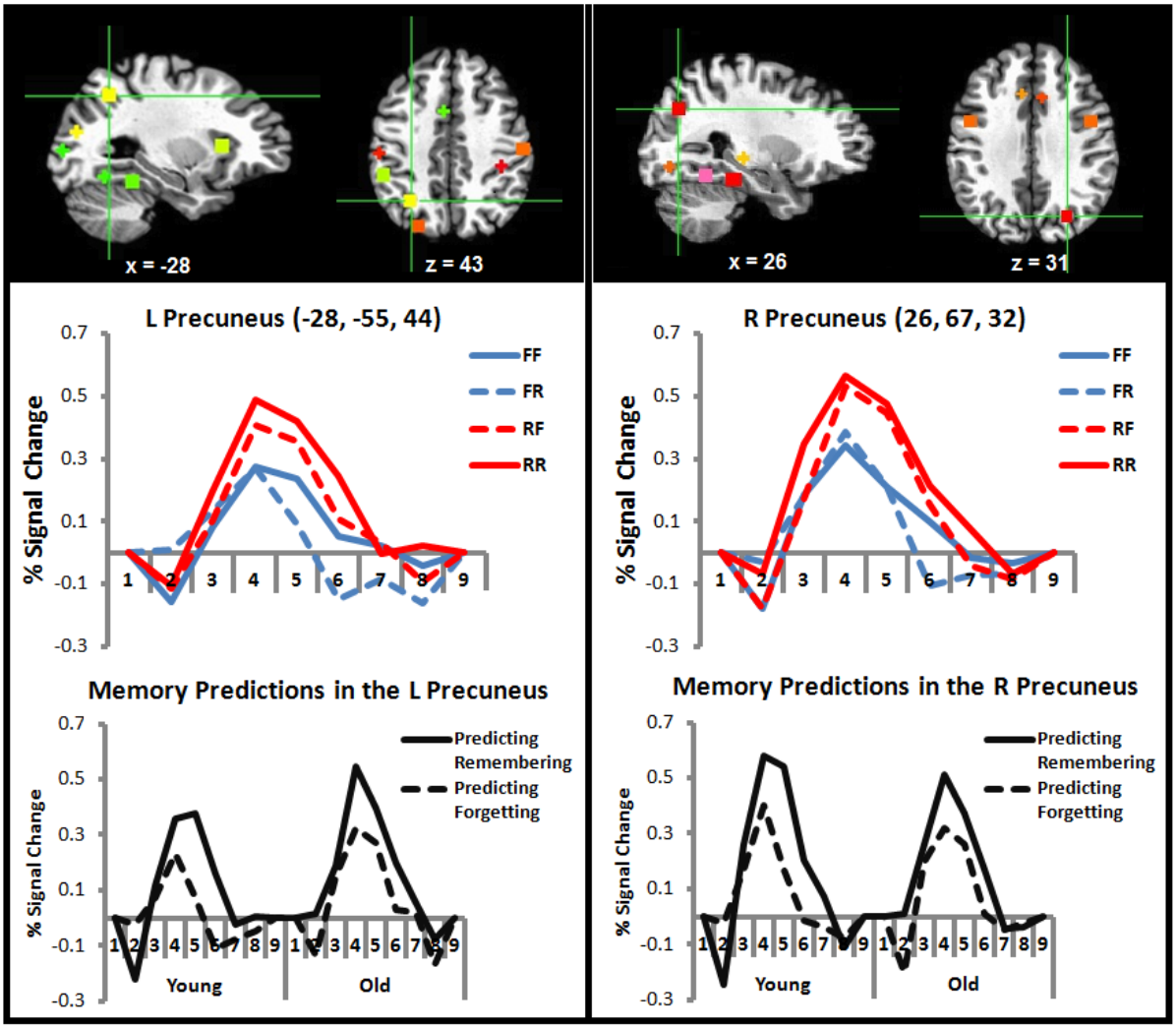

Figure 13. The hemodynamic responses function in the bilateral precuneus. The left column represents the left precuneus and the right column represents the right precuneus. The top graphs show the percent signal change for all four response types. RR and RF responses reflect "will remember" predictions, regardless of the memory performance outcome. The bottom graphs show the average of RR and RF responses and the average of FR and FF responses separate for younger and older adults. This provides a depiction of predicting remembering and predicting forgetting. One can see that this area mediates predicting remembering for both younger and older adults. *Note:* Crosshairs identify the location of the ROI. X, Y, Z coordinates are in parenthesis.

Brain regions that Mediate Encoding Success

Encoding success was classified by items that were actually remembered on the subsequent memory test, regardless of one's memory prediction (RR & FR). Using a procedure similar to that associated with identifying confidence related areas, the contrasts were executed for RR and FR versus FR and FF. The right parahippocampal gyrus (x = 26, y = -50, z = -12) had a Response x Time interaction ($F(21,5)= 6.82$, $p=.02$, $\eta p^2= .21$). The contrast looking at encoding success (RR and FR) versus encoding failure (FR and FF) was completed and rendered a significant result ($F(1, 26)=5.42$, $p = .03$; see Figure 14). Of additional interest, there was an effect of Age ($F(1,25)= 5.83$, $p=.02$, $\eta p^2= .19$), whereby younger adults had overall greater activation in the right parahippocampus. These results taken together imply that the right parahippocampal gyrus appears to mediate encoding success for both younger and older adults, with younger adults more readily activating this particular region.

The hippocampus is known for its involvement in encoding success and is also an area that is difficult to observe significant percent signal change because of both its anatomical location and its time course (Rugg et al., 2002). Consequently, an *a priori* anatomical region of interest was identified and evaluated with a less conservative threshold to further locate brain areas associated with encoding success. While the analysis was completed, the hemodynamic response function for the bilateral hippocampus did not mimic a pattern consistent with encoding, monitoring, or confidence when the relevant contrasts were performed. Although the hippocampus has been linked to encoding success previously, it is common to not see activation in this region due to the aforementioned limitations.

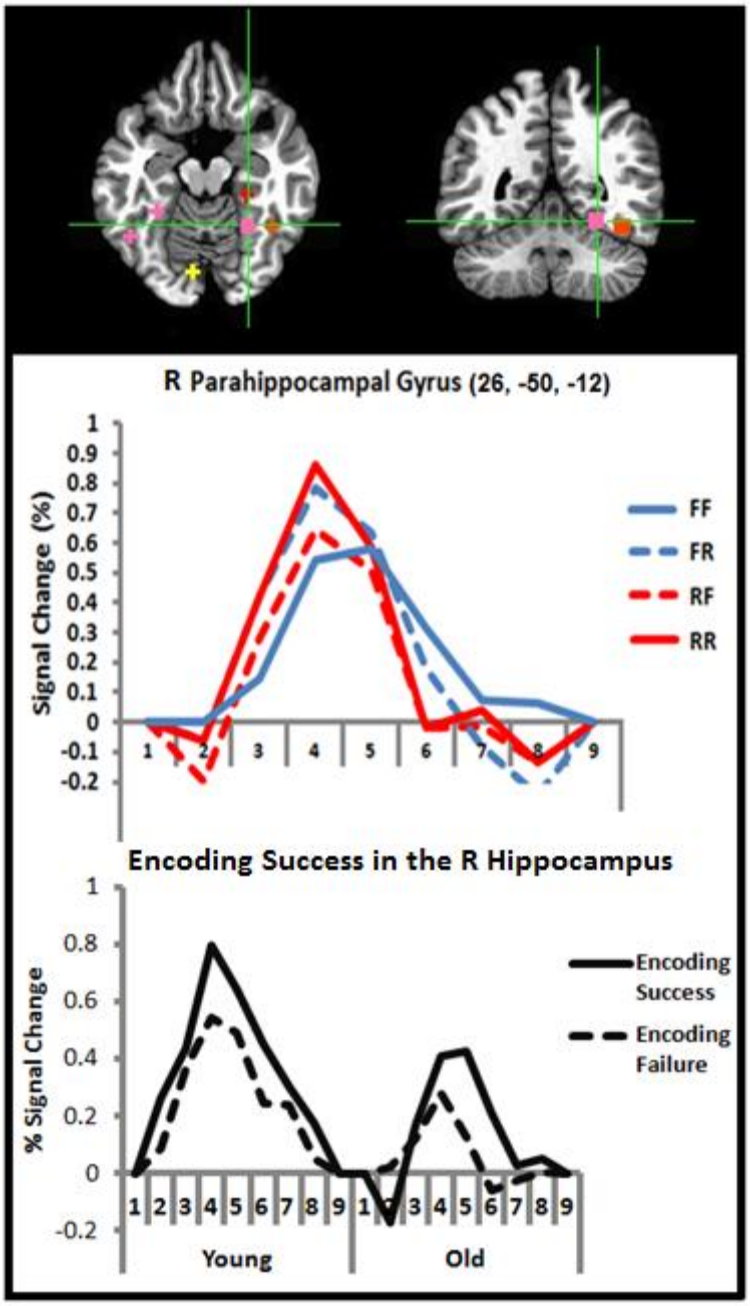

Figure 14. The hemodynamic response in the right parahippocampal gyrus. The top graphs show the percent signal change for all four response types. RR and FR responses reflect encoding success, regardless of memory prediction. The bottom graphs show the average of RR and FR responses and the average of RF and FF responses separate for younger and older adults. This provides a depiction of encoding success and encoding failure. One can see that this area mediates encoding for both younger and older adults. Crosshairs identify the location of the ROI. X, Y, Z coordinates are in parenthesis.

Brain Regions that Mediate Monitoring Accuracy

Of particular interest to the present research are areas associated with monitoring accuracy. Monitoring accuracy was defined by a pattern of responses that were associated with correctly predicting subsequent memory. That is, monitoring was considered to be accurate if one predicted forgetting and subsequently forgot that item (FF) or predicted remembering and subsequently remembered (RR) that item. In identifying regions that may be involved in monitoring accuracy, RR and FF responses were contrasted against RF and FR responses. The bilateral anterior cingulate and the right posterior cingulate were ROIs identified as being involved in monitoring accuracy.

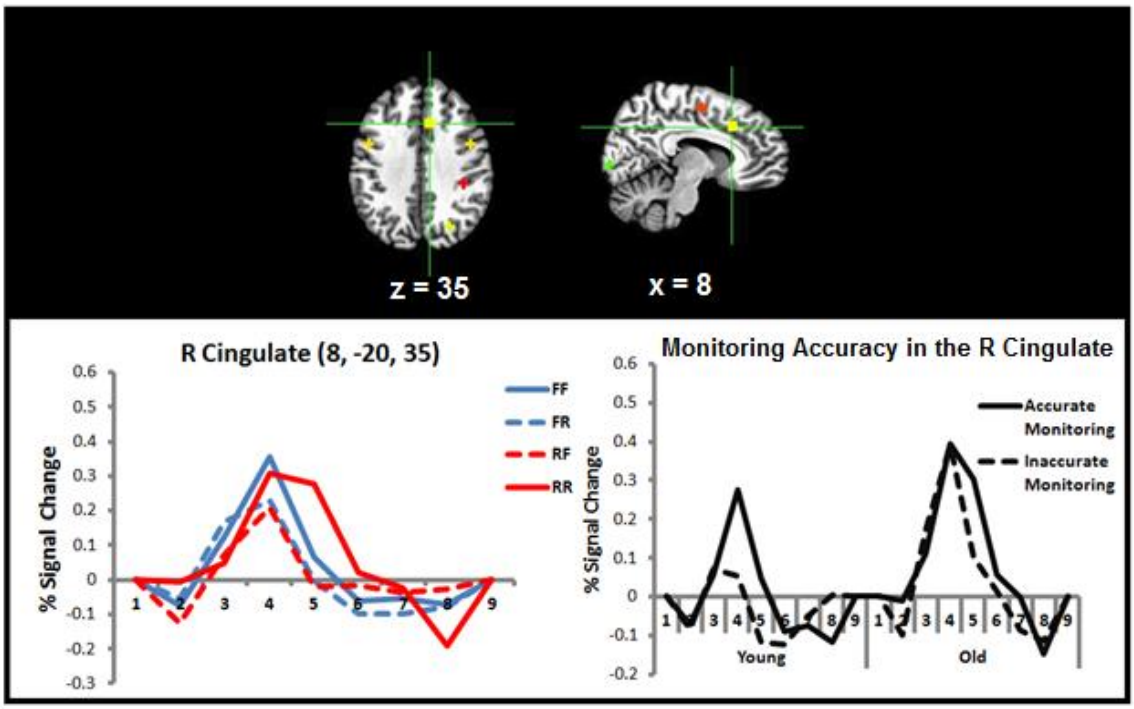

Figure 15. The hemodynamic response function in the right cingulate gyrus for all four response types. RR and FF response types reflect monitoring accuracy, regardless of memory performance. The graph on the right collapses response types across age, while the graph on the left splits the graphs by Age. Crosshairs identify the location of the ROI. X, Y, Z coordinates are in parentheses.

There was a significant Response x Time interaction in the right anterior cingulate (x = 8, y = -20, z = 35), making this region an area of interest for further contrasts (F(21, 5) =9.98, p=.01, ηp^2= .27). The right anterior cingulate varied significantly for FF and RR responses, when compared to FR and RF response (F(1, 26)=5.19, p = .03). This ROI is located in BA 32, also known for its role in performance monitoring (MacDonaldson et al., 2000). Additionally, an area in BA 32 was also identified as an ROI that mediates monitoring in Kao et al. (2005). There was a significant Age x Response interaction identified in the repeated-measures ANOVA (F(3,23) =3.99, p=.02, ηp^2= .22). When completing the same contrast for old and young adults, the older adult contrast was not significant, while the younger adult contrast was significant at (F(1, 26)=4.85, p = .04) (see Figure 15). The graphs show the hemodynamic response separate for younger and older adults, with RR and FF responses averaged to create a depiction of accurate monitoring and FR and RF responses averaged to create a depiction of inaccurate monitoring. The contrast results imply that the right anterior cingulate gyrus is not associated with monitoring accuracy for older adults, but is for younger adults.

The left anterior cingulate gyrus (x = -8, y = -23, z = 29) was also an area of interest that had a main effect of Response (F(3, 23)=7.67, p = .001, ηp^2= .42). Additionally, the overall contrast comparing RR and FF versus FR and RF was significant (F(1, 26)=5.08, p = .03) in the left cingulate gyrus and the hemodynamic response function can be observed in Figure 16. Similar to the right cingulate gyrus, this ROI is located in BA 32, an area identified in Kao et al. (2005) as being related to monitoring. Completing the same contrast separately at each Age (Young and Old) revealed that the response functions did not differ for accurate and inaccurate JOLs for

younger adults; however this contrast was significant for older adults ($F(1, 12)=9.33$, $p = .01$). This implies that activation in the left cingulate gyrus is predictive of monitoring accuracy for older adults, but not younger adults.

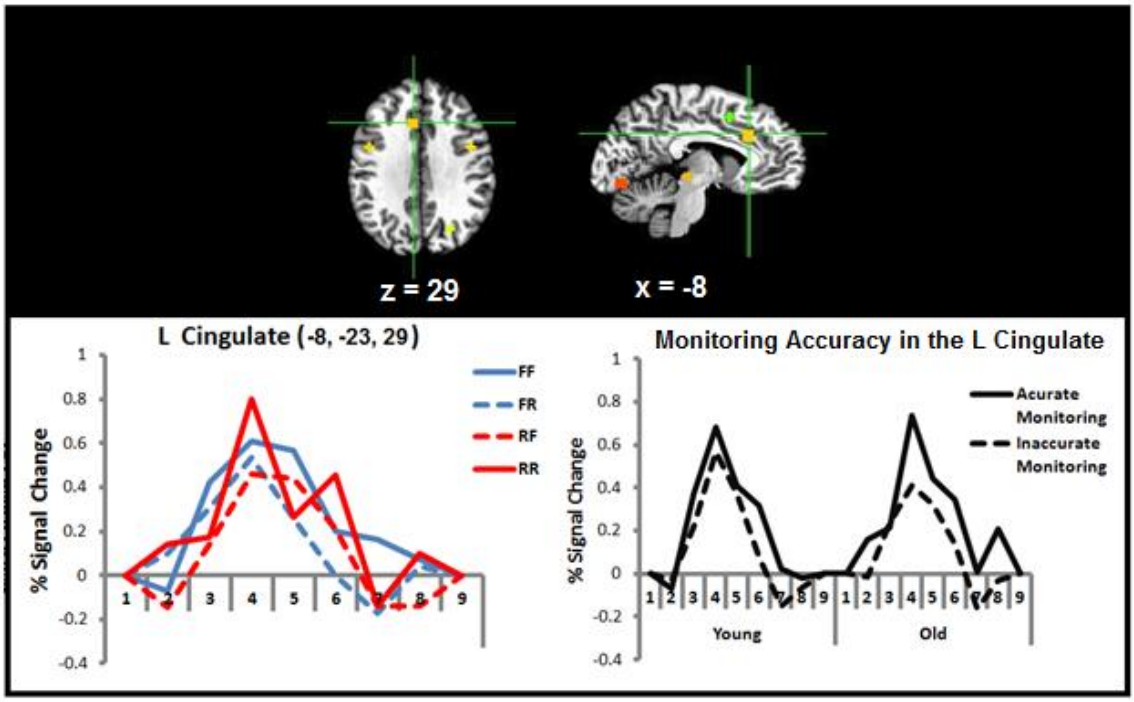

Figure 16. The hemodynamic response function in the left cingulate gyrus for all four response types. RR and FF response types reflect monitoring accuracy, regardless one's actual memory performance. The graph on the right collapses response types across age, while the graph on the left splits the graphs by age. Crosshairs identify the location of the ROI. X, Y, Z coordinates are in parenthesis.

Lastly, the right posterior cingulate (x = 18, y = 55, z = 9) was identified as a region associated with monitoring accuracy. There was a significant effect of Response; however, when the contrast RR and FF versus FR and RF was completed, it was not significant (see Figure 17). There was a significant Age x Response interaction ($F(3, 23)=9.40$, $p = .01$, $\eta p^2 = .28$), and completeing the same contrast for younger adults rendered a significant result ($F(1, 13)=6.19$, $p = .03$). For older adults, however, this statistical test was not significant, implying that the right posterior cingulate mediates monitoring for younger, but not older adults.

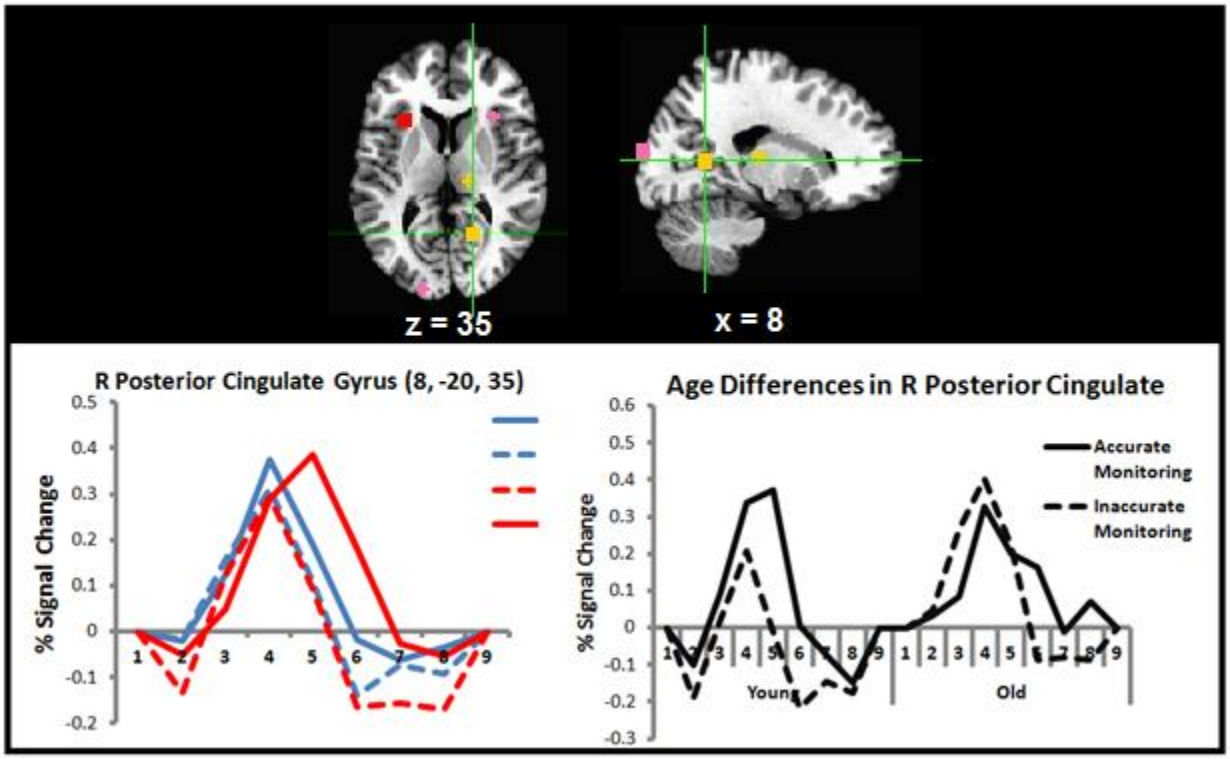

Figure 17. The hemodynamic response function in the right posterior cingulate gyrus for all four response types. RR and FF response types reflect monitoring accuracy, regardless one's actual memory performance. The graph on the right collapses response types across age, while the graph on the left splits the graphs by age. Crosshairs identify the location of the ROI. X, Y, Z coordinates are in parenthesis.

Chapter 5. Discussion

The present study intended to look at the behavioral and neurological components of monitoring during encoding, or the learning acquisition phase. This was completed by having participants predict their memory performance by providing a JOL while encoding visual scenes. Memory predictions, or JOLs, were compared to subsequent memory performance to provide a measure of monitoring accuracy. The primary purpose of the present research was to examine brain regions unique to encoding success, monitoring accuracy, and remember predictions, regardless of the difficulty of the material being learned. Because older adults are often adequate monitors, an additional goal was to disambiguate the relationship between behavioral performance and patterns of brain functioning in aging populations.

Behavioral Findings

The memory performance of older and younger adults mimicked each other, as there were no observed statistical differences in overall memory performance between age groups. Despite the overall deficits in age-related memory performance, this finding has been observed in the past, specifically for picture encoding (Gutchess et al., 2005). Both younger and older adults had a more difficult time remembering scrambled items, suggesting the difficulty manipulation worked. When considering JOL accuracy, which is synonymous here with monitoring accuracy, some interesting findings emerged. Younger adults, when compared to older adults, were better at monitoring their performance on difficult images. Older adults may have lower self efficacy, or belief in their competence, which is reflected by a shift from responding “will remember” to “will forget” specifically for difficult images. Older adults have been known to have overall lower

ratings of self efficacy (West & Thorn, 2001), which may have a detrimental effect on metamemory processes, specifically in situations that are perceived to be more difficult (Bandura, 1982; 1989). As Bandura (1989) pointed out, low measures of self-efficacy can impair metamemory functioning. Metamemory performance in the current study, as measured by JOLs, was compromised for older adults only in the more difficult condition. This was not the case for younger adults, and may be a consequence of higher feelings of self efficacy. When looking at the Memory Functioning Questionnaire (MFQ) for younger and older adults, this assertion was supported. Older adults scored lower, on average, on questions regarding their memory functioning and reported more memory problems than younger adults. Certain data patterns in the present study may also support this notion. When looking at criterion differences in response patterns, older adults were more conservative (more likely to say forget) on difficult images than younger adults. This provides additional evidence that older adults do not feel as confident in their performance given a more difficult situation. Although monitoring appears to be impaired in the difficult image condition, older adults were equivalent in performance to younger adults when averaging across image type. Given that overall monitoring performance was similar for both groups, understanding the brain-behavior relationship was the next question of interest.

Accounts of a Posterior – Anterior Shift

Because of differences in neurovasculature and white and grey matter atrophy, one must use caution when comparing the whole brain activation of younger and older adults (Rajah & D'Esposito, 2005). However, there were some findings of note that support theoretical accounts of a posterior –anterior shift associated with age. In general,

more significant clusters were identified for older adults in regions located in the frontal lobes. This is a relatively common finding in the literature and could be compensatory in nature (Dennis et al., 2008, Gutchess *et al*, 2005, Logan et al, 2002). Davis et al. (2008) demonstrated that increases in frontal activation were positively correlated with performance, but negatively correlated with occipital lobe activation (see also Gutchess et al., 2005). This implies that a decrease in posterior regions is associated with an increase in frontal lobe activation. In the present study, there were no observed behavioral or functional correlations associated with activation, likely a result of reduced power given the number of subjects, though an increased number of significant clusters in the frontal regions for older adults was still found.

Memory Predictions and the Left Precuneus

One of the primary goals of the present study was to identify brain regions that mediated the predictions of remembering, encoding success, and most importantly, monitoring accuracy. The bilateral precuneus was identified as a region associated with predicting remembering, regardless of monitoring accuracy or memory accuracy. Although the precuneus has been associated with the default network (Fransson & Marrelec, 2008), it has also been linked to high confidence judgments related to recognition memory (Chua et al., 2005). In Chua et al. (2005), while in the scanner, participants completed a recognition memory test and reported subsequent levels of confidence on the recognition memory response for each item. Similar to the current study, the intention was to separate confidence judgments (metamemory) from memory accuracy. The bilateral precuneus was more active for high confidence judgments, and to a greater degree than when recognition memory was correct. It should be noted that Chua

et al. (2005) used a retrospective judgment regarding the retrieval test phase – the present study uses prospective judgments (JOLs) during study. Kao et al. (2005), however, used similar judgments and also identified the bilateral precuneus as being associated with predicting remembering. Taken together, it does appear that the bilateral precuneus is related to performance judgments, specifically predicting both retrospective and prospective memory success, irrespective of the actual performance outcome.

Memory Accuracy and the Right Parahippocampal Gyrus

In addition to an area associated with predicting remembering, there was also an area associated with actual remembering, or encoding success. This brain region was located in the right parahippocampal gyrus, which surrounds the hippocampus and is located in the MTL. This region has been associated with encoding information, specifically for scenes (Burgman *at al*., 2010; Gutchess et al., 2005). Kao et al. (2005) reported an ROI (x = 30, y = -42, z = -19) similarly located in BA 37. Interestingly, while this area appears to mediate encoding success for both younger and older adults, younger adults activated the right parahippocampus to a greater degree. As noted, whole brain analyses comparing younger and older adults should be interpreted with caution because there are neurovasculature difference between younger and older adults that may explain some of the observed brain differences (Buckner 2004, Rajah & D'Esposito, 2005). However, reductions in the activation levels of encoding related areas in the MTL are frequently observed as one ages (Burgman *at al*., 2010; Davis et al., 2008; Gutchess et al. 2005; Park et al., 2003). Age associated reductions in MTL activation have been observed both with and without decrements in performance (Reuter-Lorenz & Cappell, 2008). In the present research, there were minimal differences in memory performance,

but older adults still activated a greater number of frontal regions when looking at whole brain group differences. This finding, taken together with decreased activation in the parahippocampus, may support an age associated compensatory mechanism, despite the adequate performance of older adults (Davis et al., 2008, Gutchess et al. 2005; Reuter-Lorenz & Cappell, 2008).

Monitoring Accuracy and the Bilateral Anterior Cingulate

The anterior cingulate (BA 32) was activated in relation to monitoring and was recruited specifically when participants were accurate in their memory predictions. That is, the anterior cingulate gyrus had increased activation when participant predictions matched their memory performance. Historically, the cingulate gyrus (specifically anterior regions) have been associated with performance monitoring (MacDonaldson et al., 2000) and goal directed behavior (Devinsky, O, Morrell, M., & Vogt, B. A., 1995). Interestingly, there were laterality differences associated with age: older adults recruited the left cingulate gyrus, while younger adults recruited the right cingulate gyrus. This is consistent with other literature in the domain of cognitive neuroscience and aging that shows older adults can recruit brain regions homologous to younger adults in the opposite hemisphere (Rajah & D'Esposito, 2005).

Similarly, Kao et al. (2005) reported the right BA 32 as an area related to monitoring accuracy. Interestingly, Kao et al. (2005) did not emphasize the cingulate gyrus as a region related to monitoring, although it was an ROI that showed greater activation when prediction matched actual performance. Although the anatomical region in the present research was located in BA 32, it is in a more posterior region of the anterior cingulate when compared to the region identified in Kao et al. (2005).

Importantly, Kao et al. (2005) only observed activation when successful encoding was predicted for an item and that item was indeed subsequently recognized (i.e., only for RR responses). The present research substantiated those findings, but was also able to identify increased activation levels in the anterior cingulate gyrus related to accurate predictions of forgetting. This is a novel result, and provides strong support that the anterior cingulate gyrus mediates monitoring accuracy, given that it was active for instances where both predicting encoding success and predicting encoding failure matched subsequent memory performance.

Monitoring Accuracy and the Right Posterior Cingulate

The right posterior cingulate was also identified as an area related to monitoring accuracy; however this was only observed for younger adults. Similar to the precuneus, the posterior cingulate has also been linked to the default network (Fransson & Marrelec, 2008). Additionally, Small, Gitelman, Gregory, Nobre, Parrish, and Mesulam (2003) found that the posterior cingulate was involved in expectancy. Specifically, they wanted to explore anticipatory responding to predictive spatial cues (valid) and non-predictive spatial cues (invalid). A cue benefit, or facilitation in reaction time, was found for valid cues and the cue benefit was associated with greater activation in the posterior cingulate. The authors concluded that the posterior cingulate is related to both motivation and attention, which are components of expectancy. For the present research, monitoring could also be related to expectancy, in that the posterior cingulate was active (only for young adults) when participant predictions, or expectations, matched their actual behavioral outcome.

The Cingulate Gyrus and Subsequent Monitoring Performance

Areas in the PFC and MTL can be used to predict subsequent memory performance (Wagner *et al*, 2008). Participants made semantic judgments (concrete or abstract) during encoding and while in the scanner. Later memory performance was assessed by a recognition test outside of the scanner. When comparing activation in encoding related areas to later memory outcomes, activation was greater in the left prefrontal and temporal cortices for stimuli that were later remembered than for those that were subsequently forgotten. Further, the ability to remember the verbal episode was predicted by the magnitude of the response in the left PFC and MTL. In a similar vein, in the current study, specific anterior and posterior regions could predict successful monitoring. Specifically, regions related to monitoring accuracy were located in the right anterior and posterior cingulate for younger adults and the left anterior cingulate for older adults. Given that these areas have been linked to the successful prediction of memory performance, it may be possible to identify which items are associated with accurate monitoring during the learning phase before a retrieval attempt is made. However, given the novelty of this research, it is necessary to further establish the role of the cingulate gyrus in monitoring accuracy and to substantiate age associated differences.

Summary of Observed Age-related Brain Differences

Brain findings can be summarized by three observations that are consistent with preexisting accounts of age-related neurological differences. First, whole brain patterns of activation were characterized by an age associated increase in the recruitment of frontal regions. Secondly, despite similarities in memory performance, there was a reduction in MTL activation for older adults but an increase in activation of frontal lobe regions,

consistent with a posterior-to-anterior shift in aging neural networks. Specifically, there was an age associated reduction in the activation of the right parahippocampal gyrus. Lastly, there were observed laterality differences between younger and older adults in the recruitment of monitoring related areas. Older adults recruited the left anterior cingulate and younger adults recruited the right anterior cingulate.

Conclusion

Importantly, distinct regions were identified and found to be unique to predicting remembering (bilateral precuneus), encoding success (right parahippocampal gyrus), and monitoring accuracy (anterior and posterior cingulate gyrus).The present research expands upon the current body of literature by providing a novel account of areas unique to monitoring memory performance in three valuable ways. First, an area associated with monitoring, the anterior cingulate, was identified as being involved in multiple aspects of monitoring accuracy. Unlike Kao et al. (2005), the anterior cingulate was activated when predicting remembering was followed by encoding success *and* when predicting forgetting was followed by encoding failure. Second, the anterior cingulate was identified as an area related to monitoring, across both easy and difficult images. Regardless of item difficulty, the anterior cingulate mediated monitoring performance. Lastly, despite similarities in behavioral performance, there were observed laterality differences in the anterior cingulate between age groups. Younger adults recruited the right anterior cingulate, while older adults recruited the left anterior cingulate. In sum, the present study established the anterior cingulate as a monitoring area for all instances of monitoring, across items varying in difficulty level, for different age groups, and identified age-related differences in the laterality of its recruitment.

Despite the lesser emphasis on monitoring in the neuroimaging literature, both encoding and monitoring are of importance during the learning of new material. The self-awareness of associated memory strategies and monitoring mechanisms have educational implications, as an assessment of successful learning can be made, and future resource allocation can be shifted based on that assessment (Connor, Dunlosky, & Hertzog, 1997; Nelson & Narens, 1990). Although poor monitors tend to have worse memory performance, monitoring strategies seem to be amenable to change, and have resulted in memory performance improvements. For example, Robinson et al. (2006) showed that individuals can be trained to use strategies through interactive imagery and other memory facilitation techniques to increase monitoring accuracy, which led to better memory performance. This is an exciting result that warrants further investigation from a neural perspective. Because the anterior cingulate was identified as a monitoring accuracy area, predictions can be made about monitoring abilities from evaluating activation in that region. The next question becomes, does providing training in strategies and resource allocation alter the recruitment of monitoring related regions? As a result of the current research, a preliminary analysis was made that connects the behavioral and neurological components of monitoring across age. Subsequent research should focus on making a connection between the behavioral and neurological components of monitoring both before and after the implementation of training.

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APPENDIX A

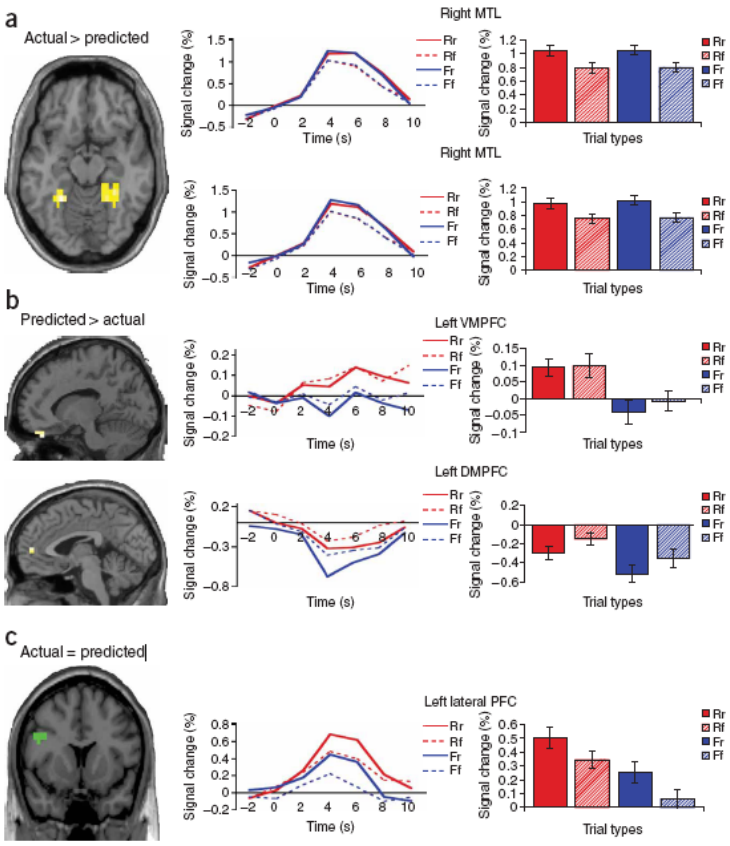


Figure 3 Statistical activation maps and percent signal change. Activation maps are rendered onto the MNI normalized canonical single-subject brain. Line graphs represent the percent signal change in brain activation as a function of time, for each of the four trial types. Bar graphs represent the mean percent signal change from 4 s to 8 s after stimulus presentation, for each of the four trial types. Error bars indicate s.e.m. R, "will remember" predictions; F, "will forget" predictions; r, later remembered; f, later forgotten. (**a**) Regions of interest (ROIs) defined from actual > predicted encoding success contrast. In bilateral medial temporal lobe (MTL), only the main effect of actual encoding success was significant (solid lines above dotted lines). (**b**) ROIs defined from predicted > actual encoding success contrast. Ventromedial prefrontal cortex (VMPFC) and dorsomedial prefrontal cortex (DMPFC) showed a significant main effect for predicted encoding success (red lines above blue lines) but not actual encoding success. However, the main effect for actual encoding success showed a trend toward significance in DMPFC. (**c**) ROIs defined from regions in which predicted encoding success matched actual encoding success. Left lateral PFC showed significant main effects for both actual and predicted encoding success. Coordinates in **Table 2**.

Results from a figure taken from Kao, Davis, & Gabrieli (2005) published in *Nature Neuroscience.*

APPENDIX B

Demographic Information

Below is a list of basic demographic questions. Please respond to the questions that you feel comfortable answering. You may skip any questions that you do not feel comfortable answering for any reason.

1. Circle one: Male or Female

2. Age:_____ Year of Birth: _____

3. Circle one that best describes your level of education:
GED
High School
Some college
Completed College
Vocational School
Graduate School
PhD/ JD/ MD

4. Circle all that apply:
Hispanic
African American
Caucasian
Native American
Asian-Pacific Islander
Other:_____

5. Are you on any medications? Circle one: YES NO
If so, please specify:_____

_____

6. How much does your physical health interfere with everyday activities of living? Please explain:_____

_____

APPENDIX C

INSTRUCTIONS: In the test that follows, the first word in each line is printed in capital letters. Opposite it are four other words. Circle the number of the ONE WORD which means the SAME THING, or most nearly the same thing, as the first word. If you don't know, guess. Be sure to choose the ONE WORD in each line that means the same thing as the first word. There are 40 questions which you will have 10 minutes to complete.

EXAMPLE:

LARGE	1) red	2) big	3) silent	4) wet

The correct response is to circle the answer (2) BIG.

When you are ready to begin, please turn the page.

APPENDIX C

SHIPLEY VOCABULARY INDEX

Please fill out the optional information in the shaded area.

Sex: M F

Age _____

How many years of education have you completed? _____

Study No. _____

Participant No.. _____

Date: _____

INDEX _____

1.	**TALK**	1) draw	2) eat	3) speak	4) sleep
2.	**PERMIT**	1) allow	2) sew	3) cut	4) drive
3.	**PARDON**	1) forgive	2) pound	3) divide	4) tell
4.	**COUCH**	1) pin	2) eraser	3) sofa	4) glass
5.	**REMEMBER**	1) swim	2) recall	3) number	4) defy
6.	**TUMBLE**	1) drink	2) dress	3) fall	4) think
7.	**HIDEOUS**	1) silvery	2) tilted	3) young	4) dreadful
8.	**CORDIAL**	1) swift	2) muddy	3) leafy	4) hearty
9.	**EVIDENT**	1) green	2) obvious	3) skeptical	4) afraid
10.	**IMPOSTOR**	1) conductor	2) officer	3) book	4) pretender
11.	**MERIT**	1) deserve	2) distrust	3) fight	4) separate
12.	**FASCINATE**	1) welcome	2) fix	3) stir	4) enchant
13.	**INDICATE**	1) defy	2) excite	3) signify	4) bicker
14.	**IGNORANT**	1) red	2) sharp	3) uninformed	4) precise
15.	**FORTIFY**	1) submerge	2) strengthen	3) vent	4) deaden
16.	**RENOWN**	1) length	2) head	3) fame	4) loyalty
17.	**NARRATE**	1) yield	2) buy	3) associate	4) tell
18.	**MASSIVE**	1) bright	2) large	3) speedy	4) low
19.	**HILARITY**	1) laughter	2) speed	3) grace	4) malice
20.	**SMIRCHED**	1) stolen	2) pointed	3) remade	4) soiled
21.	**SQUANDER**	1) tease	2) belittle	3) cut	4) waste
22.	**CAPTION**	1) drum	2) ballast	3) heading	4) ape
23.	**FACILITATE**	1) help	2) turn	3) strip	4) bewilder
24.	**JOCOSE**	1) humorous	2) paltry	3) fervid	4) plain
25.	**APPRISE**	1) reduce	2) strew	3) inform	4) delight
26.	**RUE**	1) eat	2) lament	3) dominate	4) cure

27.	**DENIZEN**	1) senator	2) inhabitant	3) fish	4) atom
28.	**DIVEST**	1) dispossess	2) intrude	3) rally	4) pledge
29.	**AMULET**	1) charm	2) orphan	3) dingo	4) pond
30.	**INEXORABLE**	1) untidy	2) involatile	3) rigid	4) sparse
31.	**SERRATED**	1) dried	2) notched	3) armed	4) blunt
32.	**LISSOM**	1) moldy	2) loose	3) supple	4) convex
33.	**MOLLIFY**	1) mitigate	2) direct	3) pertain	4) abuse
34.	**PLAGIARIZE**	1) appropriate	2) intend	3) revoke	4) maintain
35.	**ORIFICE**	1) brush	2) hole	3) building	4) lute
36.	**QUERULOUS**	1) maniacal	2) curious	3) devout	4) complaining
37.	**PARIAH**	1) outcast	2) priest	3) lentil	4) locker
38.	**ABET**	1) waken	2) ensue	3) incite	4) placate
39.	**TEMERITY**	1) rashness	2) timidity	3) desire	4) kindness
40.	**PRISTINE**	1) vain	2) sound	3) first	4) level

APPENDIX D

Memory Functioning Questionnaire

This is a questionnaire about how you remember information. There are no right or wrong answers. Circle a number between 1 and 7 that best reflects your judgment about your memory. Think carefully about your responses, and try to be as realistic as possible when you make them. Please answer all questions.

General Frequency of Forgetting

How would you rate your memory in terms of the kinds of problems that you have?

major problems			*some minor problems*			*no problems*
1	2	3	4	5	6	7

How often do these present a problem for you?

		always			*sometimes*			*never*
a.	names	1	2	3	4	5	6	7
b.	faces	1	2	3	4	5	6	7
c.	appointments	1	2	3	4	5	6	7
d.	where you put things (e.g., keys)	1	2	3	4	5	6	7
e.	performing household chores	1	2	3	4	5	6	7
f.	directions to places	1	2	3	4	5	6	7
g.	phone numbers you've just checked	1	2	3	4	5	6	7
h.	phone numbers you use frequently	1	2	3	4	5	6	7
i.	things people tell you	1	2	3	4	5	6	7
j.	keeping up correspondence	1	2	3	4	5	6	7
k.	personal dates (e.g., birthdays)	1	2	3	4	5	6	7
l.	words	1	2	3	4	5	6	7
m.	going to the store and forgetting what you wanted to buy	1	2	3	4	5	6	7
n.	taking a test	1	2	3	4	5	6	7
o.	beginning to do something and forgetting what you were doing	1	2	3	4	5	6	7
p.	losing the thread of thought in conversation	1	2	3	4	5	6	7
q.	losing the thread of thought in public speaking	1	2	3	4	5	6	7
r.	knowing whether you've already told someone something	1	2	3	4	5	6	7

How well you remember things that occurred . . .

	very bad			*fair*			*very good*
a. last month is	1	2	3	4	5	6	7
b. between 6 months and 1 year ago is	1	2	3	4	5	6	7
c. between 1 and 5 years ago is	1	2	3	4	5	6	7
d. between 6 and 10 years ago is	1	2	3	4	5	6	7

Retrospective Functioning

How is your memory compared to the way it was . . .

	much worse			*same*			*much better*
a. 1 year ago?	1	2	3	4	5	6	7
b. 5 years ago?	1	2	3	4	5	6	7
c. 10 years ago?	1	2	3	4	5	6	7
d. 20 years ago?	1	2	3	4	5	6	7
e. when you were 18?	1	2	3	4	5	6	7

Mnemonics Usage

How often do you use these techniques to remind yourself about things? . . .

	always			*sometimes*			*never*
a. keep an appointment book	1	2	3	4	5	6	7
b. write yourself reminder notes	1	2	3	4	5	6	7
c. make lists of things to do	1	2	3	4	5	6	7
d. make grocery lists	1	2	3	4	5	6	7
e. plan your daily schedule in advance	1	2	3	4	5	6	7
f. mental repetition	1	2	3	4	5	6	7
g. associations with other things	1	2	3	4	5	6	7
h. keep things you need to do in a prominent place where you will notice them	1	2	3	4	5	6	7

APPENDIX E

```
#!/bin/tcsh -xef

echo "auto-generated by afni_proc.py, Tue Nov  9 14:58:16 2010"
echo "(version 2.39, Nov 4, 2010)"

# execute via :
#   tcsh -xef S7_scriptNOV9 |& tee output.S7_scriptNOV9

# ========================== auto block: setup ============================
# script setup

# check that the current AFNI version is recent enough
afni_history -check_date 4 Nov 2010
if ( $status ) then
    echo "** this script requires newer AFNI binaries (than 4 Nov 2010)"
    echo "   (consider: @update.afni.binaries -defaults)"
    exit
endif

# the user may specify a single subject to run with
if ( $#argv > 0 ) then
    set subj = $argv[1]
else
    set subj = S7
endif

# assign output directory name
set output_dir = $subj.TENTzeroresults

# verify that the results directory does not yet exist
if ( -d $output_dir ) then
    echo output dir "$subj.results" already exists
    exit
endif

# set list of runs
set runs = (`count -digits 2 1 5`)

# create results and stimuli directories
mkdir $output_dir
mkdir $output_dir/stimuli

# copy stim files into stimulus directory
cp FF_Diff_7.1D FF_Easy_7.1D FR_Diff_7.1D FR_Easy_7.1D NR_7.1D \
    RF_Diff_7.1D RF_Easy_7.1D RR_Diff_7.1D RR_Easy_7.1D        \
    $output_dir/stimuli

# copy anatomy to results dir
3dcopy S7_structural+orig $output_dir/S7_structural
```

```
# ============================ auto block: tcat ============================
# apply 3dTcat to copy input dsets to results dir, while
# removing the first 0 TRs
3dTcat -prefix $output_dir/pb00.$subj.r01.tcat S7_run1+orig'[0..$]'
3dTcat -prefix $output_dir/pb00.$subj.r02.tcat S7_run2+orig'[0..$]'
3dTcat -prefix $output_dir/pb00.$subj.r03.tcat S7_run3+orig'[0..$]'
3dTcat -prefix $output_dir/pb00.$subj.r04.tcat S7_run4+orig'[0..$]'
3dTcat -prefix $output_dir/pb00.$subj.r05.tcat S7_run5+orig'[0..$]'

# -------------------------------------------------------
# enter the results directory (can begin processing data)
cd $output_dir


# ========================== auto block: outcount ==========================
# data check: compute outlier fraction for each volume
foreach run ( $runs )
    3dToutcount -automask -fraction -polort 3 -legendre \
                pb00.$subj.r$run.tcat+orig > outcount_r$run.1D

    # censor outlier TRs per run, ignoring the first 0 TRs
    # - censor when more than 0.15 of automask voxels are outliers
    # - step() defines which TRs to remove via censoring
    1deval -a outcount_r$run.1D -expr "1-step(a-0.15)" > rm.out.cen.r$run.1D
end

# catenate outlier counts into a single time series
cat outcount_r??.1D > outcount.rall.1D

# catenate outlier censor files into a single time series
cat rm.out.cen.r*.1D > outcount_${subj}_censor.1D

# ================================= tshift =================================
# time shift data so all slice timing is the same
foreach run ( $runs )
    3dTshift -tzero 0 -quintic -prefix pb01.$subj.r$run.tshift \
             pb00.$subj.r$run.tcat+orig
end

# ================================= align
==================================
# align anatomy to EPI registration base
align_epi_anat.py -anat2epi           \
       -anat S7_structural+orig       \
       -epi pb01.$subj.r01.tshift+orig \
       -epi_base 0 -volreg off -tshift off

# ================================= tlrc
==================================
# warp anatomy to standard space
```

```
@auto_tlrc -base TT_N27+tlrc -input S7_structural+orig -suffix NONE

# ================================= volreg
==============================
# align each dset to base volume, align to anat, warp to tlrc space

# verify that we have a +tlrc warp dataset
if ( ! -f S7_structural+tlrc.HEAD ) then
   echo "** missing +tlrc warp dataset: S7_structural+tlrc.HEAD"
   exit
endif

# create an all-1 dataset to mask the extents of the warp
3dcalc -a pb01.$subj.r01.tshift+orig -expr 1 -prefix rm.epi.all1

# register and warp
foreach run ( $runs )
   # register each volume to the base
   3dvolreg -verbose -zpad 1 -base pb01.$subj.r01.tshift+orig'[0]' \
            -1Dfile dfile.r$run.1D -prefix rm.epi.volreg.r$run     \
            -cubic                                                 \
            -1Dmatrix_save mat.r$run.vr.aff12.1D                   \
            pb01.$subj.r$run.tshift+orig

   # catenate volreg, epi2anat and tlrc transformations
   cat_matvec -ONELINE                                             \
              S7_structural+tlrc::WARP_DATA -I                     \
              S7_structural_al_mat.aff12.1D -I                     \
              mat.r$run.vr.aff12.1D > mat.r$run.warp.aff12.1D

   # apply catenated xform : volreg, epi2anat and tlrc
   3dAllineate -base S7_structural+tlrc                            \
               -input pb01.$subj.r$run.tshift+orig                 \
               -1Dmatrix_apply mat.r$run.warp.aff12.1D             \
               -mast_dxyz 3                                        \
               -prefix rm.epi.nomask.r$run

   # warp the all-1 dataset for extents masking
   3dAllineate -base S7_structural+tlrc                            \
               -input rm.epi.all1+orig                             \
               -1Dmatrix_apply mat.r$run.warp.aff12.1D             \
               -mast_dxyz 3 -final NN -quiet                       \
               -prefix rm.epi.1.r$run

   # make an extents intersection mask of this run
   3dTstat -min -prefix rm.epi.min.r$run rm.epi.1.r$run+tlrc
end

# make a single file of registration params
cat dfile.r??.1D > dfile.rall.1D
```

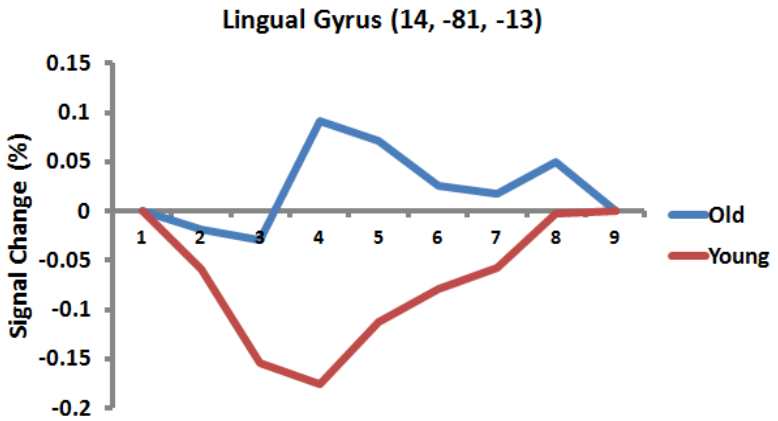
```
# ---------------------------------------
# create the extents mask: mask_epi_extents+tlrc
# (this is a mask of voxels that have valid data at every TR)
3dMean -datum short -prefix rm.epi.mean rm.epi.min.r*.HEAD
3dcalc -a rm.epi.mean+tlrc -expr 'step(a-0.999)' -prefix mask_epi_extents

# and apply the extents mask to the EPI data
# (delete any time series with missing data)
foreach run ( $runs )
    3dcalc -a rm.epi.nomask.r$run+tlrc -b mask_epi_extents+tlrc     \
           -expr 'a*b' -prefix pb02.$subj.r$run.volreg
end

# ================================== blur
==================================
# blur each volume of each run
foreach run ( $runs )
    3dmerge -1blur_fwhm 4.0 -doall -prefix pb03.$subj.r$run.blur \
            pb02.$subj.r$run.volreg+tlrc
end

# ================================== mask
==================================
# create 'full_mask' dataset (union mask)
foreach run ( $runs )
    3dAutomask -dilate 1 -prefix rm.mask_r$run pb03.$subj.r$run.blur+tlrc
end

# get mean and compare it to 0 for taking 'union'
3dMean -datum short -prefix rm.mean rm.mask*.HEAD
3dcalc -a rm.mean+tlrc -expr 'ispositive(a-0)' -prefix full_mask.$subj

# ---- create subject anatomy mask, mask_anat.$subj+tlrc ----
#      (resampled from tlrc anat)
3dresample -master full_mask.$subj+tlrc -prefix rm.resam.anat      \
           -input S7_structural+tlrc

# convert resampled anat brain to binary mask
3dcalc -a rm.resam.anat+tlrc -expr 'ispositive(a)' -prefix mask_anat.$subj

# compute overlaps between anat and EPI masks
3dABoverlap -no_automask full_mask.$subj+tlrc mask_anat.$subj+tlrc \
            |& tee out.mask_overlap.txt

# ---- create group anatomy mask, mask_group+tlrc ----
#      (resampled from tlrc base anat, TT_N27+tlrc)
3dresample -master full_mask.$subj+tlrc -prefix ./rm.resam.group   \
           -input /home/sara/abin/TT_N27+tlrc

# convert resampled group brain to binary mask
3dcalc -a rm.resam.group+tlrc -expr 'ispositive(a)' -prefix mask_group
```

```
# ================================== scale
==================================
# scale each voxel time series to have a mean of 100
# (be sure no negatives creep in)
# (subject to a range of [0,200])
foreach run ( $runs )
    3dTstat -prefix rm.mean_r$run pb03.$subj.r$run.blur+tlrc
    3dcalc -a pb03.$subj.r$run.blur+tlrc -b rm.mean_r$run+tlrc \
           -expr 'min(200, a/b*100)*step(a)*step(b)'          \
           -prefix pb04.$subj.r$run.scale
end

# ================================== regress
==================================
# run the regression analysis

# create censor file motion_${subj}_censor.1D, for censoring motion
1d_tool.py -infile dfile.rall.1D -set_nruns 5                        \
    -set_tr 2 -show_censor_count -censor_prev_TR                     \
    -censor_motion 0.5 motion_${subj}

# combine multiple censor files
1deval -a motion_${subj}_censor.1D -b outcount_${subj}_censor.1D       \
       -expr "a*b" > censor_${subj}_combined_2.1D

3dDeconvolve -input pb04.$subj.r??.scale+tlrc.HEAD                   \
    -censor censor_${subj}_combined_2.1D                             \
    -polort 3                                                        \
    -mask full_mask.S7+tlrc                                          \
    -num_stimts 15                                                   \
    -stim_times 1 stimuli/FF_Diff_7.1D 'TENTzero(0,16,9)'             \
    -stim_label 1 FF_Diff                                            \
    -stim_times 2 stimuli/FF_Easy_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 2 FF_Easy                                            \
    -stim_times 3 stimuli/FR_Diff_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 3 FR_Diff                                            \
    -stim_times 4 stimuli/FR_Easy_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 4 FR_Easy                                            \
    -stim_times 5 stimuli/NR_7.1D 'TENTzero(0,16,9)'                 \
    -stim_label 5 NR                                                 \
    -stim_times 6 stimuli/RF_Diff_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 6 RF_Diff                                            \
    -stim_times 7 stimuli/RF_Easy_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 7 RF_Easy                                            \
    -stim_times 8 stimuli/RR_Diff_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 8 RR_Diff                                            \
    -stim_times 9 stimuli/RR_Easy_7.1D 'TENTzero(0,16,9)'              \
    -stim_label 9 RR_Easy                                            \
    -stim_file 10 dfile.rall.1D'[0]' -stim_base 10 -stim_label 10 roll  \
    -stim_file 11 dfile.rall.1D'[1]' -stim_base 11 -stim_label 11 pitch \
```

```
    -stim_file 12 dfile.rall.1D'[2]' -stim_base 12 -stim_label 12 yaw   \
    -stim_file 13 dfile.rall.1D'[3]' -stim_base 13 -stim_label 13 dS    \
    -stim_file 14 dfile.rall.1D'[4]' -stim_base 14 -stim_label 14 dL    \
    -stim_file 15 dfile.rall.1D'[5]' -stim_base 15 -stim_label 15 dP    \
-fout -tout -x1D X.xmat.1D -xjpeg X.jpg                         \
    -x1D_uncensored X.uncensored.xmat.1D                            \
    -fitts fitts.$subj                                      \
    -bucket stats.$subj



# if 3dDeconvolve fails, terminate the script
if ( $status != 0 ) then
    echo '---------------------------------------'
    echo '** 3dDeconvolve error, failing...'
    echo '   (consider the file 3dDeconvolve.err)'
    exit
endif


# display any large pariwise correlations from the X-matrix
1d_tool.py -show_cormat_warnings -infile X.xmat.1D |& tee out.cormat_warn.txt

# create an all_runs dataset to match the fitts, errts, etc.
3dTcat -prefix all_runs.$subj pb04.$subj.r??.scale+tlrc.HEAD

# create ideal files for fixed response stim types
1dcat X.uncensored.xmat.1D'[20]' > ideal_FF_Diff.1D
1dcat X.uncensored.xmat.1D'[4]' > ideal_FF_Easy.1D
1dcat X.uncensored.xmat.1D'[22]' > ideal_FR_Diff.1D
1dcat X.uncensored.xmat.1D'[23]' > ideal_FR_Easy.1D
1dcat X.uncensored.xmat.1D'[24]' > ideal_NR.1D
1dcat X.uncensored.xmat.1D'[25]' > ideal_RF_Diff.1D
1dcat X.uncensored.xmat.1D'[26]' > ideal_RF_Easy.1D
1dcat X.uncensored.xmat.1D'[27]' > ideal_RR_Diff.1D
1dcat X.uncensored.xmat.1D'[28]' > ideal_RR_Easy.1D

# compute sum of non-baseline regressors from the X-matrix
# (use 1d_tool.py to get list of regressor colums)
set reg_cols = `1d_tool.py -infile X.uncensored.xmat.1D                 \
    -show_indices_interest`
3dTstat -sum -prefix sum_ideal.1D X.uncensored.xmat.1D"[$reg_cols]"

# ====================== auto block: gen_epi_review.py ======================
# generate a review script for the unprocessed EPI data
gen_epi_review.py -script @epi_review.$subj \
    -dsets pb00.$subj.r??.tcat+orig.HEAD

# ========================== auto block: cleanup ===========================
```

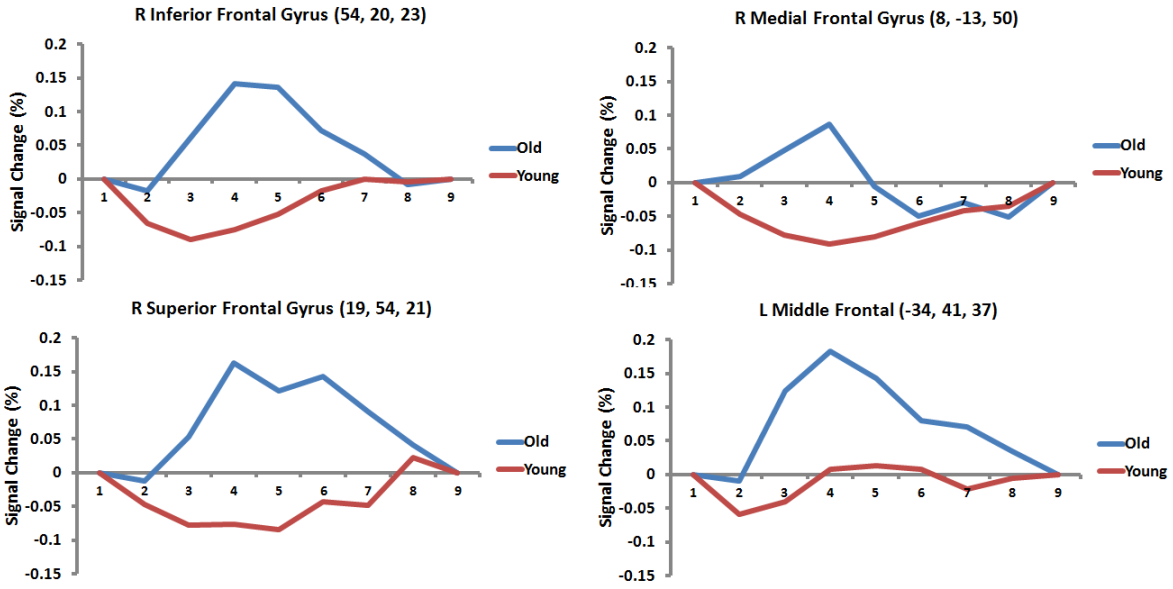
```
# remove temporary rm.* files
\rm -f rm.*

# return to parent directory
cd ..




#
============================================================================
==
# script generated by the command:
#
# afni_proc.py -do_block align tlrc -copy_anat S7_structural+orig   \
#     -volreg_tlrc_warp -volreg_align_e2a -regress_censor_motion 0.5 \
#     -regress_censor_outliers 0.15 -ask_me
#
# all applied options: -do_block align tlrc-copy_anat                        \
#     S7_structural+orig-volreg_tlrc_warp -volreg_align_e2a                  \
#     -regress_censor_motion 0.5-regress_censor_outliers 0.15-subj_id        \
#     S7-script S7_scriptNOV9-tcat_remove_first_trs 0-volreg_align_to       \
#     first-regress_basis TENTzero(0,16,9)-regress_stim_times FF_Diff_7.1D FF_Easy_7.1D  \
#     FR_Diff_7.1D FR_Easy_7.1D NR_7.1D RF_Diff_7.1D RF_Easy_7.1D        \
#     RR_Diff_7.1D RR_Easy_7.1D-regress_stim_labels FF_Diff FF_Easy FR_Diff \
#     FR_Easy NR RF_Diff RF_Easy RR_Diff RR_Easy
```

APPENDIX F



Percent signal change in the lingual gyrus. When looking at areas that produced a greater percent signal change in younger adults (Young > Old), only the lingual gyrus was significant. This area was characterized by a greater deactivation in younger adults. Response functions from the TENTzero deconvolution process were averaged at each time point and graphed separately for younger and older adults.

APPENDIX G



Percent signal change for frontal regions were Old > Young. When looking at frontal areas that produced a greater percent signal change in older adults, younger adults had deactivation in all of those areas. X, Y, Z coordinates are in parentheses.

APPENDIX H. Whole brain cluster table of Age and Difficulty

		MNI Coordinates							
		x	y	z	*t*-value	Cluster	Hemi	Region	BA
EASY	**Young > Old**	2	-104	13	17.74	36	R	Cuneus	18
		20	-69	-9	12.13	59	R	Lingual Gyrus	18
		-1	-90	-17	6.47	150	L	Lingual Gyrus	18
		20	-100	-7	5.50	21	R	Lingual Gyrus	18
		-22	-77	-27	5.00	21	L	Pyramis	
	Old > Young	-31	7	-51	13.29	18	L	Uncus	38
		-1	-81	-6	7.25	151	L	Lingual Gyrus	18
		-53	-36	20	6.20	36	L	Insula	13
		41	-44	59	5.95	276	R	Postcentral Gyrus	5
		-56	-20	17	5.91	36	L	Postcetral Gyrus	40
		-34	-56	58	5.73	126	L	Superior Parietal Lobe	7
		-49	-72	-5	5.59	146	L	Middle Occipital Gyrus	19
		54	20	23	5.54	57	R	Inferior Frontal Gyrus	9
		-28	-13	64	5.40	59	L	Precentral Gyrus	6
		-16	9	52	5.24	23	L	Medial Frontal Gyrus	6
		-10	-28	40	5.03	18	L	Cingulate	31
		-59	1	28	4.99	19	L	Precentral Gyrus	6
		5	-10	51	4.82	21	R	Medial Frontal Gyrus	6
DIFFICULT	**Young > Old**	29	-68	-19	9.13	328	R	Lingual Gyrus	18
		32	-47	-7	7.05	26	R	Parahippocampal Gyrus	37
		-24	-86	-8	6.70	30	L	Lingual Gyrus	18
		-10	-28	-38	5.33	34	L	Lingual Gyrus	19
		-16	-94	-16	5.28	377	L	Lingual Gyrus	18
	Old > Young	-22	-26	69	8.59	68	L	Postcentral Gyrus	3
		35	-47	62	6.14	102	R	Superior Parietal	7
		-53	-69	2	5.81	40	L	Middle Occipital	37
		14	-93	-14	4.89	40	R	Lingual	17
		17	-97	20	4.83	40	R	Cuneus	18
		-31	-56	58	4.68	51	L	Superior Parietal	7

Cluster table looking at Age and Item Difficulty. Second order contrasts were confined to a threshold of t= 4.61, p=.0001. The cluster size was set at 18, correcting for multiple comparisons at p=.01 *Note*: Clusters appear in order of magnitude of the *t*- values extracted from the peak voxel in each cluster. L = left, R = right.

APPENDIX I. Functionally defined ROIs identified by task versus baseline contrast

	MNI Coordinates							
ROI	**x**	**y**	**z**	***t*-value**	**Hem**	**Region**	**BA**	**Significant Interactions**
1	32	-82	6	12.76	R	Middle Occipital Gyrus	17	A × T, D × R × T
2	-32	-86	6	11.60	L	Middle Occipital Gyrus	18	D × R
3	-26	-58	-12	10.85	L	FG/Parahippocampus	19	A, A × T, R × T
4	10	-86	2	10.07	R	Middle Frontal Gyrus	11	D
5	-4	8	44	10.04	L	Medial Frontal	32	A, R, R × T
6	-28	-40	-16	9.99	L	Parahippocampal Gyrus	36	R, R × T
7	26	-50	-12	9.73	R	Parahippocampal Gyrus	37	
8	-44	-56	-10	9.22	L	FG/Parahippocampus	37	R, A × R
9	16	-94	14	9.21	R	Cuneus	18	A, D × R
10	16	92	6	9.12	L	Lingual Gyrus	17	D × R, A × T
11	32	20	6	9.09	R	Insula	13	D × R, D × R × T
12	-46	-38	42	8.86	L	Inferior Parietal Gyrus	40	A, R, D × R, A × T
13	26	31	-16	8.80	R	Middle Frontal Gyrus	11	D, D × R, R × T, A × R
14	-29	-16	9	8.78	L	Insula	13	A, R, D × A, A × R, R × T
15	26	67	32	8.69	R	Precuneus	7	R
16	41	49	-16	8.56	R	Middle Frontal Gyrus	11	R × T
17	8	-20	35	8.50	R	Cingulate Gyrus	23	A, R, D × A, D × T, A × R, D × A
18	-28	55	41	8.32	L	Superior Frontal Gyrus	9	A, R, R × T
19	-25	76	17	8.30	L	Middle Occipital Gyrus	30	A, R, A × T
20	30	73	-6	7.62	R	FG	19	D, A, D × R, A × T
21	44	-1	32	7.45	R	Precentral Gyrus	6	R, A × R, A × T, R × T, D × A × R, D × A × T
22	-43	-1	32	7.42	L	Precentral Gyrus	6	R, D, A × R
23	-8	-23	29	7.22	L	Cingulate Gyrus	6	A, R, D × A, A × R, D × A × R, D × R × T
24	-37	76	-6	7.02	L	Inferior Occipital	18	D, A, R, A × R
25	-5	25	-3	7.01	L	Anterior Cingulate	24	A, A × T, R × T
26	41	-28	17	6.76	R	Insula	13	A × R
27	23	25	-1	6.71	R	Thalamus/Hippocampus	27	R × T, D × A × R
28	-19	28	3	6.54	L	Thalamus/Hippocampus	27	A × R, R × T, D × R × T, A × R × T, D × A × R × T
29	14	22	11	6.53	R	Thalamus		A, R, A × R, R × T, D × R × T
30	18	55	9	6.34	R	Posterior Cingulate	30	D, A, R, D × A, D × R, A × R, R × T, D × R × T
31	53	19	41	6.23	R	Middle Frontal Gyrus	6	D, A, D × R, R × T
32	-22	73	41	6.05	L	Precuneus	19	A, R, A × T
33	-8	76	-10	6.01	L	Declive	17	
34	4	7	51	5.82	R	Superior Frontal Gyrus	6	D, A, D × R, A × T, R × T
35	35	13	62	5.73	R	Middle Frontal Gyrus	6	A, R
36	-49	22	45	5.71	L	Middle Frontal Gyrus	8	A, A × R, A × T, R × T, D × R × T
37	38	31	38	5.67	R	Middle Frontal Gyrus	8	A, R, A × T, R × T, D × A, R
38	-34	8	17	5.62	L	Insula	13	A, D × R, A × T

Functionally defined ROIs. ROIs were identified by contrasting task versus baseline at a threshold of t=5.507, p=.00001. The time course was obtained for each ROI and was submitted to a 2 (Age) x 2 (Difficulty) x 4 (Response) x 9 (Time) repeated measures ANOVA. Results from this analysis are reported in the Significant Effects column. The x,y,z coordinates and t-value are reported for the peak voxel within each ROI. The radius

of each ROI was set at 5mm and a separation of 10mm from the voxel with the peak activation. *Note*: Regions of interest (ROIs) appear in order of magnitude of the maxima used to identify the original ROI. Hem = hemisphere; L = left; R = right; FG = Fusiform Gyrus; A = age; T = Time; R = Response; D = Difficulty.